

# **EXHIBIT 33**

**Food and Drug Administration Office of Regulatory Affairs****Summary Report****For Sample Number: 448881****TD Sample Number:****Import Sample Number**

This is an accurate reproduction of the original electronic record as of 04/30/2008

Sample Class: Normal Everyday Sample  
Survey Sample

Sample Origin: Domestic

Sample Basis: Surveillance

Sample Type: Official

Collecting District: DET-DO

Home District:

Orig C/R and Records To: DAL-DO

Collection PACs: 56008A

Product Name: Digoxin (Cardiotonic); Human - Rx/Single Ingredient; Prompt Release Tablets

Product Description: 100 x 0.125mg Digoxin Tablets, USP

Collection Reason: The sample was collected as per memo for the FY 2008 Low Cost Generic Drug Sample Survey # 2008-800 (CP 7356.008) and is being reported in FACTS under Assignment # 896688 and Op # 3518058.

Lab: NRL	Split Num 0	Date Received: 12/18/2007	Date Out of Lab: 04/29/2008
District		District Conclusion	District
Conclusion:		Made By:	
Disposition		Disposition	Disposition
Reason:		Authorized By:	Authorized Date

Performing Org	PAC	LID	PAF	Compliance No	Lab Class-Description	Laboratory Status
NRL-DCB-G	56008A		DRT		1 - In Compliance	Completed

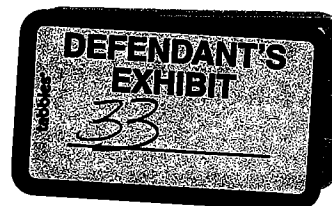
**Lab Conclusion**

The product meets specifications for Identification, Dissolution and Content Uniformity.

**Lab Conclusion Date****Lab Conclusion Made By**

04/30/2008

Mathew, Samuel K



DAL-DO

**Food and Drug Administration Office of Regulatory Affairs  
Collection Report**

**For Sample Number: 448881**

This is an accurate reproduction of the original electronic record as of 12/14/2007

<b>Flag</b>	<b>Flag Remarks</b>				
Survey Sample	FY 2008 Low Cost Generic Drug Sample Survey # 2008-800				
<b>Episode Number</b>	<b>Origin</b>	<b>Basis</b>	<b>Sample Type</b>	<b>FIS Smpl Num</b>	<b>Status</b>
	Domestic	Surveillance	Official	0882632	Completed
<b>FEI</b>	<b>Date Collected</b>	<b>Product Code</b>	<b>Responsible Firm</b>	<b>PAC</b>	<b>Hours</b>
1610608	12/03/2007	63FCA06	Shipper	56008A	2
<b>Compliance Num</b>	<b>Country of Origin</b>				
	United States				
<b>Related Smpl Num</b>	<b>Position Class</b>	<b>Sampling District</b>	<b>NDC Number</b>	<b>Permit Number</b>	<b>Storage Rqrmnt.</b>
	INV	DET-DO	62794-145-01		Ambient
<b>Dealer Is Consumer</b>	<b>Crx/DEA Schedule</b>	<b>Recall Num</b>	<b>Consumer Compl. Num</b>	<b>Brand Name</b>	
No				Digitek	

**Product Description**

100 x 0.125mg Digoxin Tablets, USP

**Product Label**

See continuation.

**Reason for Collection**

The sample was collected as per memo for the FY 2008 Low Cost Generic Drug Sample Survey # 2008-800 (CP 7356.008) and is being reported in FACTS under Assignment # 896688 and Op # 3518058.

**MFG Codes**

70298A1

**Expiration Date**

April 2009

<b>Firm Legal Name</b>	<b>Address</b>	<b>Type of Firm</b>	<b>Firm FEI</b>	<b>FCE</b>
UDL Laboratories, Inc	12720 Dairy Ashford Rd Sugar Land, TX 77478-2844 US	Shipper	1610608	
Actavis Totowa LLC	101 E Main St Little Falls, NJ 07424-5608 US	Manufacturer	2244683	
Wal-Mart Pharmacy Warehouse #6028	801 Corda Blvd Crawfordsville, IN 47933-2152 US	Dealer	3004344335	
<b>Size of Lot</b>	<b>Est. Value</b>	<b>Rept Type</b>	<b>Carrier Name</b>	<b>Date Shipped</b>
(b) (4) x 100 count bottles		FDA484		

**Description of Sample**

See continuation.

**Method of Collection**

2 x 100 count bottles of Digitek (Digoxin Tablets, USP) lot 70298A1 were randomly selected from shelf.

**How Prepared**

See continuation.

**Collector's Identification on Package and/or Label**

"Sample # 448881 EB 12/3/07"

**Collector's Identification on Seal**

"448881 Ernest Bizjak 12/3/07"

**Sample Delivered To**

FEDEX

**Date Delivered**

12/17/2007

**Orig C/R & Records To**

DAL-DO

**Lab w/Split Sample**

0

**Lab**

NRL

**Document Number****Document Date**

12.03/2007

**Document Type**

Other

**Document Remarks**

FDA-482; 1 page

Date: 12/14/2007

Page: 1 of 3

**Food and Drug Administration Office of Regulatory Affairs**

**Collection Report**

**For Sample Number: 448881**

This is an accurate reproduction of the original electronic record as of 12/14/2007

12/03/2007

Other

FDA-484; 4 pages

**Remarks**

See continuation.

**Payment Amount**

**Payment Method**

**704(d) Sample**

**702(b) Portion**

**Collector's Name**

No Charge

No

No

Ernest Bizjak

**Name of Signer**

**Date & Time of Signature**

**Meaning**

Ernest Bizjak

12/14/2007

09:12 AM

ET

Collector

**Food and Drug Administration Office of Regulatory Affairs  
Collection Report**

**For Sample Number: 448881**

This is an accurate reproduction of the original electronic record as of 12/14/2007

**Continuation:**

**Product Label**

The white HDPE bottles with matching screw caps are labeled in part "NDC 62794-145-01 \*\*\* DIGITEK \*\*\* (digoxin tablets, USP) 125 mcg (0.125mg) \*\*\* 100 TABLETS \*\*\* Rx only \*\*\* Distributed by: BERTEK PHARMACEUTICALS INC. Sugar Land, TX 77478 USA \*\*\* Manufactured by: AMIDE PHARMACEUTICALS, INC. 101 East Main Street Little Falls, NJ 07424 USA \*\*\* Control No.: 70298A1 \*\*\* Exp. Date: APR 09".

**Description of Sample**

The sample consists of 2 x 100 count bottles 0.125mg Digitek (Digoxin Tablets, USP) NDC # 62794-145-01 assigned lot # 70298A1 and expiry date April 2009.

**How Prepared**

The 2 bottles were identified as per Collector's ID and placed into a clear Whirl-pak bag that was then officially sealed at the dealer. The sample was transported back to the DET-DO/INDY-RP where it was stored in a locked sample cabinet at ambient conditions until it was boxed and shipped to lab.

**Remarks**

Per assignment memo, test samples for UDU, Diss, and ID. All analytical methods are compendial.

Dena McClamroch, General Manager stated that she could not provide a dollar value for the sample. If this information is needed, contact Monty Mason, Pharmacy Director at ph#479-277-1558.



DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION		1. DISTRICT OFFICE ADDRESS & PHONE NO. DET. DIS # 32-342-8100 300 Ann Arbor St. S.W. Detroit MI 48207	
2. NAME AND TITLE OF INDIVIDUAL Dena M. McQuinn		3. DATE 12/3/07	
4. FIRM NAME Wal-Mart		5. HOUR 9:25 a.m.	
6. NUMBER AND STREET 801 Cor-dea Blvd.		5. HOUR p.m.	
7. CITY AND STATE & ZIP CODE Crawfordsville, IN 47933		8. PHONE # & AREA CODE (765) 361-1192	

Notice of Inspection is hereby given pursuant to Section 704(a)(1) of the Federal Food, Drug, and Cosmetics Act [21 U.S.C. 374(a)]<sup>1</sup> and/or Part F or G, Title III of the Public Health Service Act [42 U.S.C. 262-264]<sup>2</sup>

9. SIGNATURE (Food and Drug Administration Employee(s))

*[Signature]*

10. TYPE OR PRINT NAME AND TITLE (FDA Employee(s))

Ernest Bizjak, Investigator

<sup>1</sup> Applicable portions of Section 704 and other Sections of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 374] are quoted below:

Sec. 704. (a)(1) For purposes of enforcement of this Act, officers or employees duly designated by the Secretary, upon presenting appropriate credentials and a written notice to the owner, operator, or agent in charge, are authorized (A) to enter, at reasonable times, any factory, warehouse, or establishment in which food, drugs, devices, or cosmetics are manufactured, processed, packed, or held, for introduction into interstate commerce or after such introduction, or to enter any vehicle being used to transport or hold such food, drugs, devices, or cosmetics in interstate commerce; and (B) to inspect, at reasonable times and within reasonable limits and in a reasonable manner, such factory, warehouse, establishment, or vehicle and all pertinent equipment, finished and unfinished materials, containers, and labeling therein. In the case of any factory, warehouse, establishment, or consulting laboratory in which prescription drugs, nonprescription drugs intended for human use, or restricted devices are manufactured, processed, packed, or held, inspection shall extend to all things therein (including records, files, papers, processes, controls, and facilities) bearing on whether prescription drugs, nonprescription drugs intended for human use or, restricted devices which are adulterated or misbranded within the meaning of this Act, or which may not be manufactured, introduced into interstate commerce, or sold, or offered for sale by reason of any provision of this Act, have been or are being manufactured, processed, packed, transported, or held in any such place, or otherwise bearing on violation of this Act. No inspection authorized by the preceding sentence or by paragraph (3) shall extend to financial data, sales data other than shipment data, pricing data, personnel data (other than data as to qualifications of technical and professional personnel performing functions subject to this Act), and research data (other than data relating to new drugs, antibiotic drugs and devices and, subject to reporting and inspection under regulations lawfully issued pursuant to section 505(i) or (k), section 507(d) or (g), section 519, or 520(g), and data relating to other drugs or devices which in the case of a new drug would be subject to reporting or inspection under lawful regulations issued pursuant to section 505(j) of the title). A separate notice shall be given for each such inspection, but a notice shall not be required for each entry made during the period covered by the inspection. Each such inspection shall be commenced and completed with reasonable promptness.

Sec. 704(e) Every person required under section 519 or 520(g) to maintain records and every person who is in charge or custody of such records shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and to copy and verify, such records.

Section 704 (f)(1) A person accredited under section 523 to review reports made under section 510(k) and make recommendations of initial classifications of devices to the Secretary shall maintain records documenting the training qualifications of the person and the employees of the person, the procedures used by the person for handling confidential information, the compensation arrangements made by the person, and the procedures used by the person to identify and avoid conflicts of interest. Upon the request of an officer or employee designated by the Secretary, the person shall permit the officer or employee, at all reasonable times, to have access to, to copy, and to verify, the records.

Section 512 (1)(1) In the case of any new animal drug for which an approval of an application filed pursuant to subsection (b) is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to experience, including experience with uses authorized under subsection (a)(4)(A), and other data or information, received or otherwise obtained by such applicant with respect to such drug, or with respect to animal feeds bearing or containing such drug, as the Secretary may by general regulation, or by

order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) or subsection (m)(4) of this section. Such regulation or order shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulation or order is applicable, of similar information received or otherwise obtained by the Secretary.

(2) Every person required under this subsection to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

<sup>2</sup> Applicable sections of Parts F and G of Title III Public Health Service Act [42 U.S.C. 262-264] are quoted below:

Part F - Licensing - Biological Products and Clinical Laboratories and\*\*\*\*\*

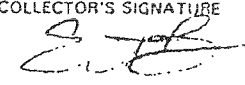
Sec. 351(c) "Any officer, agent, or employee of the Department of Health & Human Services, authorized by the Secretary for the purpose, may during all reasonable hours enter and inspect any establishment for the propagation or manufacture and preparation of any virus, serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or other product aforesaid for sale, barter, or exchange in the District of Columbia, or to be sent, carried, or brought from any State or possession into any other State or possession or into any foreign country, or from any foreign country into any State or possession."

Part F - \*\*\*\*\*Control of Radiation.

Sec. 360 A(a) "If the Secretary finds for good cause that the methods, tests, or programs related to electronic product radiation safety in a particular factory, warehouse, or establishment in which electronic products are manufactured or held, may not be adequate or reliable, officers or employees duly designated by the Secretary, upon presenting appropriate credentials and a written notice to the owner, operator, or agent in charge, are thereafter authorized (1) to enter, at reasonable times any area in such factory, warehouse, or establishment in which the manufacturer's tests (or testing programs) required by section 358(h) are carried out, and (2) to inspect, at reasonable times and within reasonable limits and in a reasonable manner, the facilities and procedures within such area which are related to electronic product radiation safety. Each such inspection shall be commenced and completed with reasonable promptness. In addition to other grounds upon which good cause may be found for purposes of this subsection, good cause will be considered to exist in any case where the manufacturer has introduced into commerce any electronic product which does not comply with an applicable standard prescribed under this subpart and with respect to which no exemption from the notification requirements has been granted by the Secretary under section 359(a)(2) or 359(e)."

(b) "Every manufacturer of electronic products shall establish and maintain such records (including testing records), make such reports, and provide such information, as the Secretary may reasonably require to enable him to determine whether such manufacturer has acted or is acting in compliance with this subpart and standards prescribed pursuant to this subpart and shall, upon request of an officer or employee duly designated by the Secretary, permit such officer or employee to inspect appropriate books, papers, records, and documents relevant to determining whether such manufacturer has acted or is acting in compliance with standards prescribed pursuant to section 359(a)."

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DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		1. DISTRICT ADDRESS & PHONE NUMBER DET - DO # 313 - 393 - 8100 300 River Place, Suite 5900 Detroit, MI 48207	
2. NAME AND TITLE OF INDIVIDUAL Dena M. McClamroch, General Manager		3. DATE 12/3/07	4. SAMPLE NUMBER *See below
5. FIRM NAME Wal-Mart		6. FIRM'S DEA NUMBER	
7. NUMBER AND STREET 201 Cor-dea Blvd.		8. CITY AND STATE (Include Zip Code) Cincinnati, IN 47933	
9. SAMPLE COLLECTED (Describe fully. List lot, serial, model numbers and other positive identification)  The following samples were collected by the Food and Drug Administration and receipt is hereby acknowledged pursuant to Section 704(c) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 374(c)) and / or Section 532 (b) of the Federal Food, Drug, and Cosmetic Act (21 USC 360i(b)) and/or 21 Code of Federal Regulations (CFR) 1307.02. Excerpts of these are quoted on the reverse of this form. (NOTE: If you bill FDA for the cost of the Sample(s) listed below, please attach a copy of this form to your bill.) Sample #414920 consists of (1) 2 x 100 bottles Captopril Tablets, 12.5mg, lot DG10952 with NDC # (b) (4) (2) Sample #414931 consists of 53 x 3.5g tubes Erythromycin Ophthalmic Ointment, 5mg/g, lot P53 with NDC # (b) (4) (3) Sample #414932 consists of 2x100 bottles Hydrochlorothiazide capsules, 12.5mg, lot 350713 with NDC # (b) (4) (4) Sample #414933 consists of 2x100 bottles Estradiol Tablets, 0.5mg, lot 304344 with NDC # (b) (4) (5) Sample #414934 consists of 2x100 bottles Atenolol Tablets, 25mg, lot 151437 with NDC # (b) (4) (6) Sample #414935 consists of 1x500 bottle Amoxicillin Capsules, 250mg, lot # 022011 with NDC # (b) (4) (7) Sample #414936 consists of 2x100 bottles Enoxaparin Sodium Tablets, 2.5mg, lot # 27875 with NDC # (b) (4) (8) Sample #414937 consists of 22 bottles Amoxicillin for Oral Suspension, 200mg/5mL, lot # 1755794, NDC # (b) (4)			
10. SAMPLES WERE <input checked="" type="checkbox"/> PROVIDED AT NO CHARGE <input type="checkbox"/> PURCHASED <input type="checkbox"/> BORROWED (To be returned)		11. AMOUNT RECEIVED FOR SAMPLE <input checked="" type="checkbox"/> CASH <input type="checkbox"/> BILLED <input type="checkbox"/> VOUCHER <input type="checkbox"/> CREDIT CARD	
12. SIGNATURE (Persons receiving payment for sample or person providing sample to FDA at no charge.) Dena McClamroch		13. COLLECTOR'S NAME (Print or Type) Emma B...	
14. COLLECTOR'S TITLE (Print or Type) Inventory		15. COLLECTOR'S SIGNATURE 	

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		1. DISTRICT ADDRESS & PHONE NUMBER DET. DO #313-393-8100 300 River Place, Suite 5900 Detroit, MI 48207	
2. NAME AND TITLE OF INDIVIDUAL Dana M. McClunoch, General Manager		3. DATE 12/3/07	4. SAMPLE NUMBER See below *
5. FIRM NAME Wib-Start		6. FIRM'S DEA NUMBER	
7. NUMBER AND STREET 201 Cor-de Blvd.		8. CITY AND STATE (Include Zip Code) Crawfordsville, IN 47933	
9. SAMPLE COLLECTED (Describe fully. List lot, serial, model numbers and other positive identification)  The following samples were collected by the Food and Drug Administration and receipt is hereby acknowledged pursuant to Section 704(c) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 374(c)) and / or Section 532 (b) of the Federal Food, Drug, and Cosmetic Act (21 USC 360i(b)) and/or 21 Code of Federal Regulations (CFR) 1307.02. Excerpts of these are quoted on the reverse of this form. (NOTE: If you bill FDA for the cost of the Samples listed below, please attach a copy of this form to your bill.)  <p>① Clonidine ER 12/1/07</p> <p>⑨ Sample #448877 consists of 3x90 boxes Clonidine HCl Tablets, 0.1mg, lot 7141833, NDC # (b) (4)</p> <p>⑩ Sample #448878 consists of 2x100 bottles Bupropion Extended Release / Hydrochlorothiazide Tablets, 2.5/6.25mg, lot 1508006 with NDC # (b) (4)</p> <p>⑪ Sample #448879 consists of 53x15g tubes Guanine Sulfate Ointment, 0.1%, lot Z176 with NDC # (b) (4)</p> <p>⑫ Sample #448880 consists of 2x100 bottles Glyburide Tablets, 2.5mg, lot 1493474 with NDC # (b) (4)</p> <p>⑬ Sample #448881 consists of 2x100 bottles Digitek (Digoxin) Tablets, 0.125mg, lot 70298A1 with NDC - 62794-145-01</p> <p>⑭ Sample #448882 consists of 7x30 bottles Cefaloprim HBr Tablets, 200mg, lot C72275 with NDC # (b) (4)</p> <p>⑮ Sample #448883 consists of 83x5mL bottles Guanine Sulfate Ophthalmic Solution, 3mg/mL, lot 129553F with NDC # (b) (4)</p> <p>⑯ Sample #448884 consists of 2x100 bottles Ciprofloxacin Tablets, 250mg, lot # 717002 with NDC # (b) (4)</p>			
10. SAMPLES WERE <input checked="" type="checkbox"/> PROVIDED AT NO CHARGE <input type="checkbox"/> PURCHASED <input type="checkbox"/> BORROWED (To be returned)		11. AMOUNT RECEIVED FOR SAMPLE <input checked="" type="checkbox"/> No <input type="checkbox"/> CASH <input type="checkbox"/> BILLED <input type="checkbox"/> VOUCHER <input type="checkbox"/> CREDIT CARD	
12. SIGNATURE (Persons receiving payment for sample or person providing sample to FDA at no charge.) Dana McClunoch		13. COLLECTOR'S NAME (Print or Type) Ernest Bujak	
14. COLLECTOR'S TITLE (Print or Type) Inspector		15. COLLECTOR'S SIGNATURE [Signature]	



DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		1. DISTRICT ADDRESS & PHONE NUMBER DET. DO # 313-393-8100 300 River Place, S.W. Detroit, MI 48207	
2. NAME AND TITLE OF INDIVIDUAL Dennis M. McVimruch, General Manager		3. DATE 12/3/07	4. SAMPLE NUMBER *see below
5. FIRM NAME V. V. V. - Mkt		6. FIRM'S DEA NUMBER	
7. NUMBER AND STREET 201 Cedar Blvd.		8. CITY AND STATE (Include Zip Code) Cedar Rapids, IA 52403	
9. SAMPLE COLLECTED (Describe fully. List lot, serial, model numbers and other positive identification)  The following samples were collected by the Food and Drug Administration and receipt is hereby acknowledged pursuant to Section 704(c) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 374(c)) and / or Section 532 (b) of the Federal Food, Drug, and Cosmetic Act (21 USC 360(b)) and/or 21 Code of Federal Regulations (CFR) 1307.02. Excerpts of these are quoted on the reverse of this form. (NOTE: If you bill FDA for the cost of the Sample(s) listed below, please attach a copy of this form to your bill.)			
(17) Sample # 448885 consists of 2x100 bottles Euthicon Tablets, 250 mg, lot 567534F22 with NDC # (b) (4)			
(18) Sample # 448886 consists of 2x100 bottles Acyclovir Capsules, 200 mg, lot 35300555A with NDC # (b) (4)			
(19) Sample # 448887 consists of 2x100 bottles Bactrimide Tablets, 0.5 mg, lot 1V76033 with NDC # (b) (4)			
(20) Sample # 448888 consists of 2x100 bottles Doxazosin Mesylate Tablets 1 mg, lot 3000793 with NDC # (b) (4)			
(21) Sample # 448889 consists of 2x100 bottles Fentanyl Tablets, 20 mg, lot BEB02A with NDC # (b) (4)			
(22) Sample # 448890 consists of 53x2.5g tubes Bactrim Ophthalmic Ointment, 500 U/g lot P72 with NDC # (b) (4)			
(23) Sample # 448891 consists of 54x2.0ml bottles Albuterol Sulfate Inhalation Solution, 0.5%, lot 157641, with NDC # (b) (4)			
(24) Sample # 448892 consists of 2x100 bottles Digoxin Tablets, 0.25 mg, lot 7C66441 with NDC # 62794-146-01			
10. SAMPLES WERE <input checked="" type="checkbox"/> PROVIDED AT NO CHARGE <input type="checkbox"/> PURCHASED <input type="checkbox"/> BORROWED (To be returned)		11. AMOUNT RECEIVED FOR SAMPLE <input checked="" type="checkbox"/> CASH <input type="checkbox"/> BILLED <input type="checkbox"/> VOUCHER <input type="checkbox"/> CREDIT CARD	
12. SIGNATURE (Persons receiving payment for sample or person providing sample to FDA at no charge.) Dennis M. McVimruch		13. COLLECTOR'S NAME (Print or Type) Ernest Bujak	
14. COLLECTOR'S TITLE (Print or Type) Investigator		15. COLLECTOR'S SIGNATURE 	

<b>DÉPARTMENT OF HEALTH AND HUMAN SERVICES</b> <b>PUBLIC HEALTH SERVICE</b> <b>FOOD AND DRUG ADMINISTRATION</b>		1. DISTRICT ADDRESS & PHONE NUMBER DET. DO #313-392-8100 300 River Place, Suite 550 Detroit, MI 48207	
2. NAME AND TITLE OF INDIVIDUAL Denis M. McNamee, General Manager		3. DATE 12/2/07	4. SAMPLE NUMBER *see below*
5. FIRM NAME Wal-Mart		6. FIRM'S DEA NUMBER	
7. NUMBER AND STREET 801 Corcoran Blvd.		8. CITY AND STATE (Include Zip Code) Evansville, IN 47933	
9. SAMPLE COLLECTED (Describe fully. List lot, serial, model numbers and other positive identification)  <p>The following samples were collected by the Food and Drug Administration and receipt is hereby acknowledged pursuant to Section 704(c) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 374(c)] and / or Section 532 (b) of the Federal Food, Drug, and Cosmetic Act [21 USC 360i(b)] and/or 21 Code of Federal Regulations (CFR) 1307.02. Excerpts of these are quoted on the reverse of this form.          (NOTE: If you bill FDA for the cost of the Sample(s) listed below, please attach a copy of this form to your bill.)</p> <p>(25) Sample # 448893 consists of 2x100 bottles Diltiazem HCL Tablets, 20mg, lot 201047 with NDC # (b) (4)</p> <p>(26) Sample # 448894 consists of 1x1000 bottles Amitriptyline HCL Tablets, 10mg, lot 1P7678 with NDC # (b) (4)</p> <p>(27) Sample # 448895 consists of 2x100 bottles (b) (4) (Carbamazepine) Tablets, 200mg, lot 211870 with NDC # (b) (4)</p> <p>(28) Sample # 448896 consists of 2x100 bottles Fluoxetine Capsules, 10mg, lot 148748A with NDC # (b) (4)</p> <p>These samples were provided free of charge.</p>			
10. SAMPLES WERE <input checked="" type="checkbox"/> PROVIDED AT NO CHARGE <input type="checkbox"/> PURCHASED <input type="checkbox"/> BORROWED (To be returned)		11. AMOUNT RECEIVED FOR SAMPLE <input checked="" type="checkbox"/> No charge <input type="checkbox"/> CASH <input type="checkbox"/> BILLED <input type="checkbox"/> VOUCHER <input type="checkbox"/> CREDIT CARD	
12. SIGNATURE (Persons receiving payment for sample or person providing sample to FDA at no charge.) Denis M. McNamee		13. COLLECTOR'S NAME (Print or Type) Frank B. York	
14. COLLECTOR'S TITLE (Print or Type) Investigator		15. COLLECTOR'S SIGNATURE ETE	

FLAG Original

<b>ANALYST WORKSHEET</b>		1. PRODUCT DIGITEK (digoxin tablets, USP) 125 mcg (0.125 mg)		2. SAMPLE NUMBER 448881	
3. SEALS <input type="checkbox"/> NONE <input checked="" type="checkbox"/> INTACT <input type="checkbox"/> BROKEN		4. DATE REC'D 2/4/08		5. RECEIVED FROM Howard Lynch	
6. DISTRICT OF LABORATORY NRL					
7. DESCRIPTION OF SAMPLE  One clear, plastic bag officially sealed, "448881 12/3/07 Ernest Bizjak Investigator", containing two product bottles each identified "448881 ES 12/3/07". An FDA 525 is attached to the sample.					
8. NET CONTENTS  <input type="checkbox"/> NOT APPLICABLE <input checked="" type="checkbox"/> NOT DETERMINED <input checked="" type="checkbox"/> UNITS EXAMINED		DECLARE/UNIT 100 tablets AMOUNT FOUND _____ % OF DECLARED _____		9. LABELING  1 ORIGINAL(S) SUBMITTED ____ COPIES SUBMITTED <input type="checkbox"/> NONE	
10. SUMMARY OF ANALYSIS  Container: Round, opaque, white, plastic bottle with a similar, screw-on, safety cap. Safety-seal beneath cap is intact. Bottle is approximately 4 cm. in diameter and 7.5 cm. in height.  Labeling: Commercially-printed, rectangular, paper, stick-on label. Commercially-printed product insert is inside bottle.  Code: " Control No.: 70298A1 " and " Exp. Date: APR 09 " printed on each bottle label.  Product: Round, flat and bevel, solid, light-yellow tablet. Tablet is unmarked and unscored on one side. Opposite side is 1/2-scored with markings "B" and "145". Tablet is approximately 6.5 mm in diameter.  Analysis: Identification, Dissolution, and Content Uniformity.  Method: USP 30 - NF 25, p. 1943.  Results: See general continuation sheet page 2.					
11. RESERVE SAMPLE  Original plastic bag containing one open and one intact product bottle. Bag is officially sealed " 448881 4/23/08 Valentino Fiorella Analyst". Open bottle is identified " 448881 VF 2/4/08 " and " DPD 4/23/08 ". Sample returned to the sample custodian.					
12.a. ANALYST SIGNATURE (Broken Seal <input checked="" type="checkbox"/> ) <i>Valentino Fiorella</i>		13. WORK-SHEET CHECK		a. BY <i>S. Matthew</i>	
b. <i>Dongping Dai</i>				b. DATE 4/29/08	
c.				14. DATE REPORTED 4/29/08	

VF 4/29/08

GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets (0.125 mg)	SAMPLE NO. 448881
----------------------------	---------------------------------------	----------------------

**RESULTS:**

**Identification**

The retention time of the major peak in the chromatogram of the sample preparation corresponds to that in the chromatogram of the standard preparation. Complies

**Content Uniformity**  
(See computer printout pages 6 - 7 for complete results)

Range: 98.8 % to 102.2 %; Average (X): 100.2 %;  
RSD: 1.1 %; s: 1.13

Acceptance Value (AV) = 2.7 %

(Limit: AV ≤ 15.0 % unless otherwise specified in the individual monograph)

**Dissolution**  
(See least squares line fitting page // for complete results)

Range: 91.3 % to 108.0 % ; Avg.: 98.4 %

(Limit: Each unit is NLT Q+5% (Q=80%) for 6 units tested (Stage 1))

ANALYST(S) <i>Valentino J. Farrell</i>	ANALYST NO. 113	PAGE <u>2</u> OF <u>11</u> PAGES
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FORM FDA 431a (5/84)



SPL# 445881  
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VF

DIGOXIN TABLETS

(USP 30-NF 25, p.1943)

Reference Std:

USP Digoxin RS # 1200000-05, Lot 00B096, dried in vacuum at 105°C for 1 hour prior to use. For quantitative applications, use a value of 0.961 mg of digoxin per mg on the dried basis.

Reagents: Fisher Scientific Acetonitrile, Lot 073938 (REC'D 11/10/07 ARS)  
Sigma Digoxigenin, Lot No. 016K3777 (REC'D 2/14/08 ESW)

Filter: PALL Life Sciences Acrodisc 25 mm Syringe Filter with 0.45 um Nylon Membrane, Lot A10529577

Identification

The retention time of the major peak in the chromatogram of the sample preparation corresponds to that in the chromatogram of the standard preparation. Complete

Content Uniformity

Mobile Phase: Water/Acetonitrile (74/26)

System Suitability Solution

(Balance: Cahn C-31 Microbalance, FDA No. 5004472 - QA by G.Lehr on 1/14/08)

4.025 mg USP Digoxin RS + 4.122 mg Digoxigenin

----> 100.0 ml Diluted Alcohol

Standard Solution 1 (CCV)

(Balance: Cahn C-31 Microbalance, FDA No. 5004472 - QA by G.Lehr on 1/14/08)

2.522 mg USP Digoxin RS ----> 100.0 ml Diluted Alcohol

25.0 ml

-----> 50.0 ml Diluted Alcohol

Standard Solution 2 (ICV/Check Std.)

(Balance: Cahn C-31 Microbalance, FDA No. 5004472 - QA by G.Lehr on 1/14/08)

2.505 mg USP Digoxin RS ----> 100.0 ml Diluted Alcohol

25.0 ml

-----> 50.0 ml Diluted Alcohol

GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets (0.125 mg)	SAMPLE NO. 448881
ANALYST(S) <i>Valentino Fucile</i>	ANALYST NO. 113	PAGE 3 OF 11 PAGES

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### Content Uniformity

#### Sample Solution

For each of 10 tablets tested:

1 tablet (0.125 mg) ----> 10.0 ml Diluted Alcohol ---> Filter

#### Chromatographic System

(See pp. 2 - 3 , Attachment A for chromatograms)

#### Resolution (R)

$$R = \frac{2(t_2 - t_1)}{w_1 + w_2} = \frac{2.11}{\quad} \quad [\text{Limit: } R \text{ is NLT } 4.0]$$

#### Theoretical Plates (N)

$$N = 16(t/w)^2 = \frac{5949}{\quad} \quad [\text{Limit: } N \text{ is NLT } 1200]$$

#### Tailing Factor (T)

$$T = [W_{0.05}/2F] = \frac{1.2}{\quad} \quad [\text{Limit: } T \text{ is NMT } 2.0]$$

#### Relative Std. Deviation (RSD)

(See computer calculation, page 5 )

$$RSD = \frac{0.27}{\quad} \% \quad [\text{Limit: } RSD \text{ is NMT } 2.0\%]$$

#### Standard 2 Calculation (ICV/Check Std.)

(See pp. 3 - 8 , Attachment A for chromatograms)

$$\% \text{ Digoxin} = \frac{\text{Area Std. 2}}{\text{Area Std. 1}} \times \frac{\text{Std 1 Wt.}}{\text{Std 1 Dilution}} \times \frac{\text{Std 2 Dilution}}{\text{Std 2 Wt.}} \times 100$$

Area Std. 1 = Avg. area of 5 std. injections. (See computer calculation, p. 5 )

$$\text{Std. Wt. 1} = (2.522 \text{ mg}) (0.961) = 2.424 \text{ mg}$$

$$\text{Std. Wt. 2} = (2.505 \text{ mg}) (0.961) = 2.407 \text{ mg}$$

$$\% \text{ Digoxin} = \frac{673965}{682162} \times \frac{2.424 \text{ mg}}{200.0 \text{ ml}} \times \frac{200.0 \text{ ml}}{2.407 \text{ mg}} \times 100 = \frac{99.5}{\quad} \%$$

GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets (0.125 mg)	SAMPLE NO. 448881
ANALYST(S) <i>Valentino J. Furell</i>	ANALYST NO. 113	PAGE 4 OF 11 PAGES

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#### Standard 1 Calculation (CCV)

(See pp. 3 - 7 and page 20, Attachment A for chromatograms)

$$\% \text{ Digoxin} = \frac{\text{Area Std.1} (7)}{\text{Area Std.1}} \times \frac{\text{Std 1 Wt.}}{\text{Std 1 Dilution}} \times \frac{\text{Std 1 Dilution}}{\text{Std 1 Wt.}} \times 100$$

Area Std.1 = Avg. area of 5 std. injections. (See computer calculation, p. 5)  
 Area Std.1 (7) = Area of Std.1, Injection 7. (See page 20, Attachment A)  
 Std.Wt.1 = (2.522 mg)(0.961) = 2.424 mg

$$\% \text{ Digoxin} = \frac{6818.35}{68216.2} \times \frac{2.424 \text{ mg}}{200.0 \text{ ml}} \times \frac{200.0 \text{ ml}}{2.424 \text{ mg}} \times 100 = 100.0\%$$

#### Calculations

(See computer printout pages 6 - 7 for complete results and pages 9 - 13, Attachment A for chromatograms)  
 + 15-19

Area Std.1 = Avg. area of 5 std. injections. (See computer calculation, p. 5)  
 Std.Wt.1 = (2.522 mg)(0.961) = 2.424 mg

If  $98.5\% \leq X \leq 101.5\%$ , then  $M = X$

Range: 98.8% to 102.2%; Average (X): 100.2%; RSD: 1.1%; s: 1.13

$$\text{Acceptance Value (AV)} = M - X + ks = (2.4) (1.13) = 2.71\%$$

(Limit: AV  $\leq$  15.0 % unless otherwise specified in the individual monograph)



General Continuation  
Sheet

Product: Digoxin Tablets (0.125 mg)

Sample No. 448881

## Statistical Analysis of Data:

Standard Solution 1 (CCV)

02/14/2008

Relative STD Deviation	0.27 %		
Standard Deviation	1847.90944		
Average (mean)	682161.6		
Number of entries	5		
Range	680386	To	684459

## Data Entered:

680386  
681506  
683776  
684459  
680681

Analyst(s)

*Valentino J. F. L.*

Analyst No.

113

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General Continuation  
Sheet

Product: Digoxin Tablets

Sample No. 448881

## Content Uniformity

02/15/2008

No. of Units Examined	10
Standard Weight	2.424 mg.
Standard Dilution	200
Sample Dilution	10

## Data Entered:

Unit #1	713065	STD #1	682162
Unit #2	702312	Blank	0
Unit #3	695180		
Unit #4	701285		
Unit #5	711091		
Unit #6	708580		
Unit #7	698918		
Unit #8	707409		
Unit #9	718912		
Unit #10	695739		

## CONTENT UNIFORMITY RESULTS:

	FOUND ( mg/tablet )	DECLARED	% of DECLARED
UNIT #1	0.127	0.125	101.4
UNIT #2	0.125	mg/tablet	99.8
UNIT #3	0.124		98.8
UNIT #4	0.125		99.7
UNIT #5	0.126		101.1
UNIT #6	0.126		100.7
UNIT #7	0.124		99.3
UNIT #8	0.126		100.5
UNIT #9	0.128		102.2
UNIT #10	0.124		98.9
AVG.	0.125		100.2

OFFICIAL LIMITS: 90.0 % TO 105.0 %  
 No. of Units Examined 10  
 RANGE 98.8 % TO 102.2 % of Declared  
 UNITS  $\geq 85$  BUT  $\leq 115$  % of Avg. Limit : 10  
 UNITS  $\geq 75$  BUT  $< 85$  OR  $> 115$  BUT  $\leq 125$  % of Avg. Limit : 0  
 UNITS  $< 75$  OR  $> 125$  % of Avg. Limit : 0  
 REL. STD. DEV. : 1.1 LIMIT  $\leq 6.0\%$

$$\text{mg/unit} = (R_{\text{spl}} * \text{std\_wt} * \text{spl\_dil}) / (R_{\text{std}} * \text{std\_dil} * 1 \text{ unit})$$

Analyst(s)

*Valentino Fiorell*Analyst No.  
113

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General Continuation  
Sheet

Product: Digoxin Tablets (0.125 mg)

Sample No. 448881

**Statistical Analysis of Data:**Content Uniformity  
Standard Deviation

02/15/2008

Relative STD Deviation	1.12 %		
Standard Deviation	1.13		
Average (mean)	100.24		
Number of entries	10		
Range	98.8	To	102.2

## Data Entered:

101.4  
99.8  
98.8  
99.7  
101.1  
100.7  
99.3  
100.5  
102.2  
98.9

Analyst(s)

*Valentino Fiorella*Analyst No.  
113

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GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets (0.125 mg)	SAMPLE NO. 448881
ANALYST(S) <i>Valentino J. Torelli</i>	ANALYST NO. 113	PAGE 8 OF 11 PAGES

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Dissolution

Medium: 0.1N HCl, 500 ml (37.0°C ± 0.5°C)

Apparatus 1: 120 rpm

Time: 60 minutes

Instrument: Distek Dissolution Apparatus #1, FDA No. 1218  
(QA by R.Muzeni on 4/9/08)

Instrument: Shimadzu Fluorescence Spectrophotometer, FDA# 5004459  
(QA by V.Fiorella on 1/11/08)

Reagents: Sigma L-Ascorbic Acid, Lot 10K0256 (REC'D BEFORE 4/10/06)  
Sigma-Aldrich 30% Hydrogen Peroxide, Batch# 04824AH (REC'D 4/3/08)  
Burdick & Jackson Methanol, Lot CU893 (REC'D 12/20/07)  
Fisher Scientific Hydrochloric Acid, Lot 068102 (REC'D 5/4/07)

Ascorbic acid-Methanol Solution

(Mettler Toledo AX205, FDA No. 5099471 - QA by A.Stewart on 1/10/08)

201.7 mg Ascorbic acid ----> 100.0 ml MeOH

Hydrogen peroxide-Methanol Solution

Stock Solution: 2.0 ml 30% H<sub>2</sub>O<sub>2</sub> ---> 100.0 ml MeOH (Refrigerate)

Working Solution: 2.0 ml Stock ---> 100.0 ml MeOH

Standard Solutions

(Cahn C-31 Microbalance, FDA No. 5004472 - QA by G.Lehr on 1/14/08)

Stock Solution

25.079 mg USP Digoxin RS ---> 500.0 ml Dilute Alcohol (4 in 5)

10.0 ml  
-----> 100.0 ml Dilute Alcohol (4 in 5) [0.005 mg/ml]



GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets (0.125 mg)	SAMPLE NO. 448881
ANALYST(S) <i>Valentino-Lirell</i>	ANALYST NO. 113	PAGE 9 OF 11 PAGES

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### Working Standard Solutions

Standard Solution	ml Stock Solution	ml Dissolution Medium	Final Concentration (mg/ml)
20%	1.0	100.0	0.00005
40%	2.0	100.0	0.00010
60%	3.0	100.0	0.00015
80%	2.0	50.0	0.00020
100%	5.0	100.0	0.00025

Test Solution (6 tablets tested; 0.125 mg/tablet)

1 tablet ---> 0.1N HCl, 500 ml ---> Filter [0.00025 mg/ml]

### Procedure

Test Prep.: 1.0 ml Test Solution (Prepared in duplicate)  
 + 1.0 ml Ascorbic acid-Methanol Solution  
 + 5.0 ml HCl  
 + 1.0 ml Hydrogen peroxide-Methanol Solution

----> Glass-stoppered flask

Std. Preps.: 1.0 ml of each Working Std. Solution  
 + 1.0 ml Ascorbic acid-Methanol Solution  
 + 5.0 ml HCl  
 + 1.0 ml Hydrogen peroxide-Methanol Solution

----> Glass-stoppered flask

Blank Prep.: 1.0 ml Dissolution Medium  
 + 1.0 ml Ascorbic acid-Methanol Solution  
 + 5.0 ml HCl  
 + 1.0 ml Hydrogen peroxide-Methanol Solution

----> Glass-stoppered flask

GENERAL CONTINUATION SHEET	PRODUCT Digoxin Tablets (0.125 mg)	SAMPLE NO. 448881
ANALYST(S) <i>Valentino Fiorell</i>	ANALYST NO. 113	PAGE <i>10</i> OF <i>11</i> PAGES

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V.F

### Procedure

After 2 hours (FDA Timer# 1678), measure the fluorescence of each preparation at an emission wavelength of about 485 nm and an excitation wavelength of about 372 nm correcting each reading for the blank.

Plot a standard curve of Fluorescence vs. % Dissolution.

Determine the % dissolution of digoxin for each Test Solution from the graph.

### Results

See least squares line fitting page // for complete results and Attachment B for spectra.

Tablet	Avg. % Dissolution
1	91.25
2	96.7
3	92.35
4	96.35
5	107.95
6	105.9
Avg. (6 Tablets)	98.4

[Limit: Each unit is NLT  $Q + 5\%$  ( $Q=80\%$ ) for 6 units tested (Stage 1)]

General Continuation  
Sheet

Product: Digoxin Tablets (0.125 mg)

Sample No.

448881

## Least Squares Line Fitting

04/24/2008

The Line Fitting used is  $Y = mX + b$ with  $m =$  0.019795and  $b =$  -0.0745

Correlation Coefficient = 0.99911

Data Entered:

X	Y	LSLF y	% Deviation
20	0.352	0.3214	9.521
40	0.676	0.7173	5.758
60	1.109	1.1132	0.377
80	1.519	1.5091	0.656
100	1.91	1.905	0.262

Extrapolated Data:

	X	Y
Tab 1	90.8	1.723
	91.7	1.740
Tab 2	96.2	1.829
	97.2	1.850
Tab 3	90.8	1.722
	93.9	1.785
Tab 4	95.5	1.815
	97.2	1.850
Tab 5	111.8	2.138
	104.1	1.987
Tab 6	105.0	2.003
	106.8	2.039

Analyst(s) *Dongping Dai*Analyst No.  
000

Page // of // Pages



ATTACHMENT A - Page / of 20 pages

Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: Blank

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\Blank-Rep2

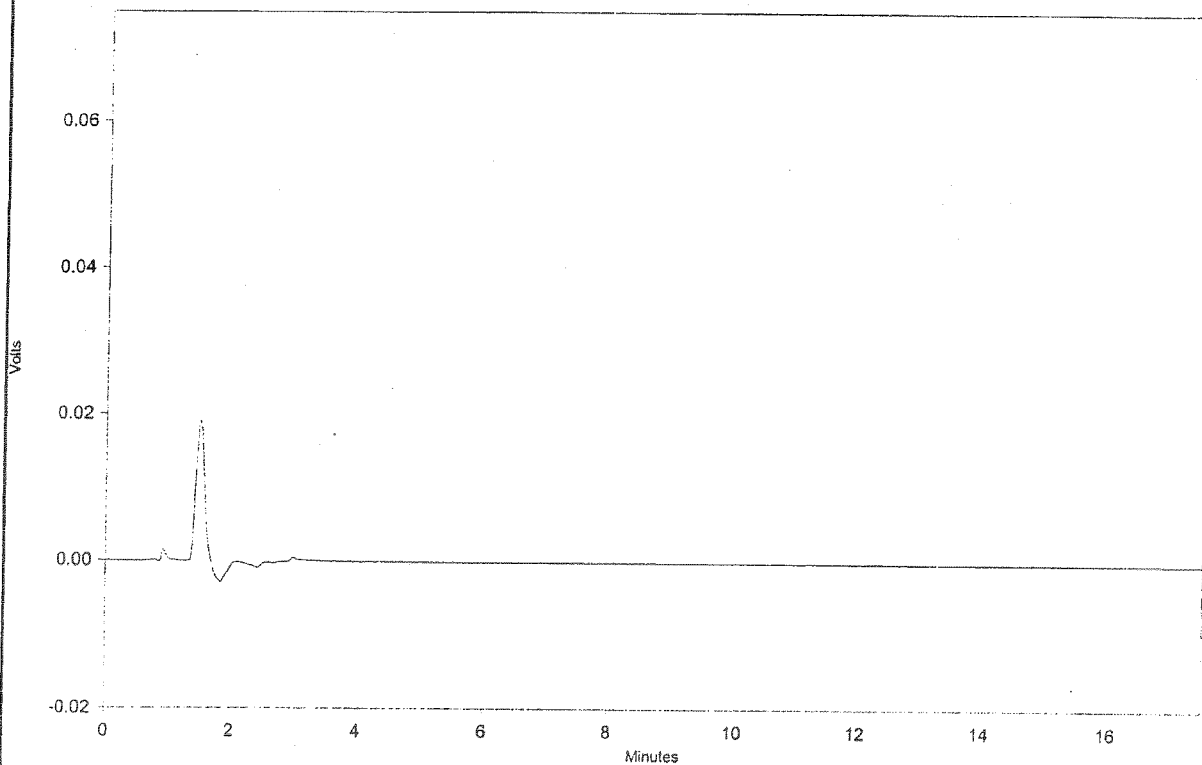
Date: 02/14/2008 7:34:08 AM

Vial: 0

Injection Volume: 50 ul

Detector A  
(218nm)

PK #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates



Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C

ATTACHMENT A - Page 2 of 20 pages

Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: System Suitability Solution

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\SysSuitSoln

Date: 02/14/2008 7:53:05 AM

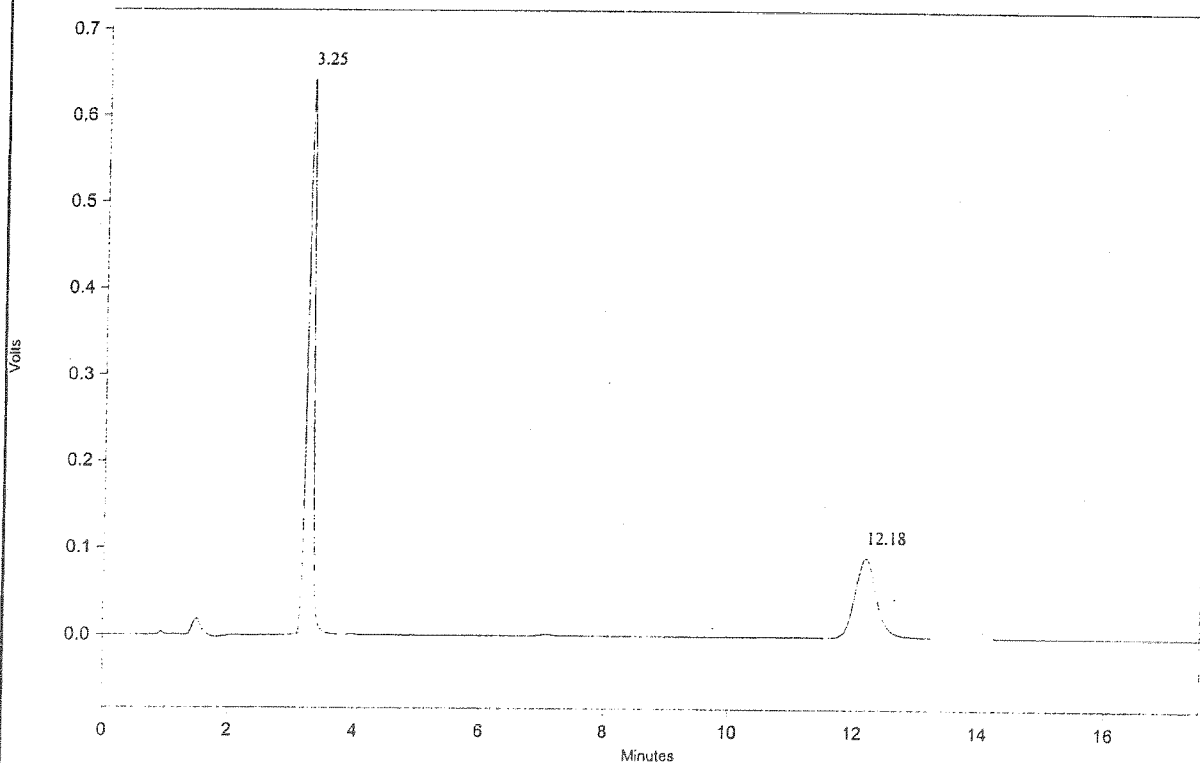
Vial: 1

Injection Volume: 50 ul

Detector A  
(218nm)

PK #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates
1	Digoxigenin	3.25	4401132	642009	1.2	0.0	3384
2	Digoxin	12.18	2206126	91863	1.2	21.1	6132

Totals			6607258	733872			
--------	--	--	---------	--------	--	--	--



Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C

ATTACHMENT A - Page 3 of 20 pages

Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: Standard Solution 1 (CCV)

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\Std.Soln-Rep1

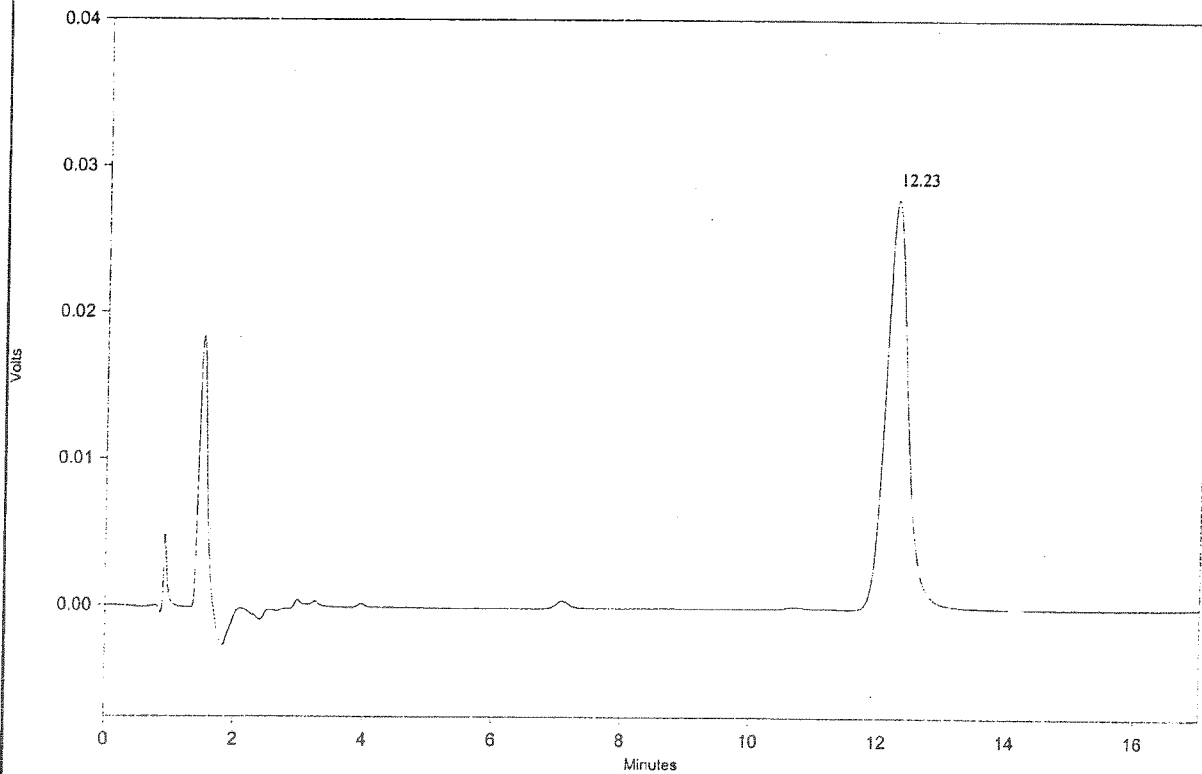
Date: 02/14/2008 8:15:55 AM

Vial: 2

Injection Volume: 50 ul

Detector A  
(218nm)

Pk #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates
1	Digoxin	12.23	680386	27974	1.2	0.0	5949
Totals			680386	27974			



Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C

ATTACHMENT A - Page 4 of 20 pages

Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: Standard Solution 1 (CCV)

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\Std.Soln-Rep2

Date: 02/14/2008 8:34:23 AM

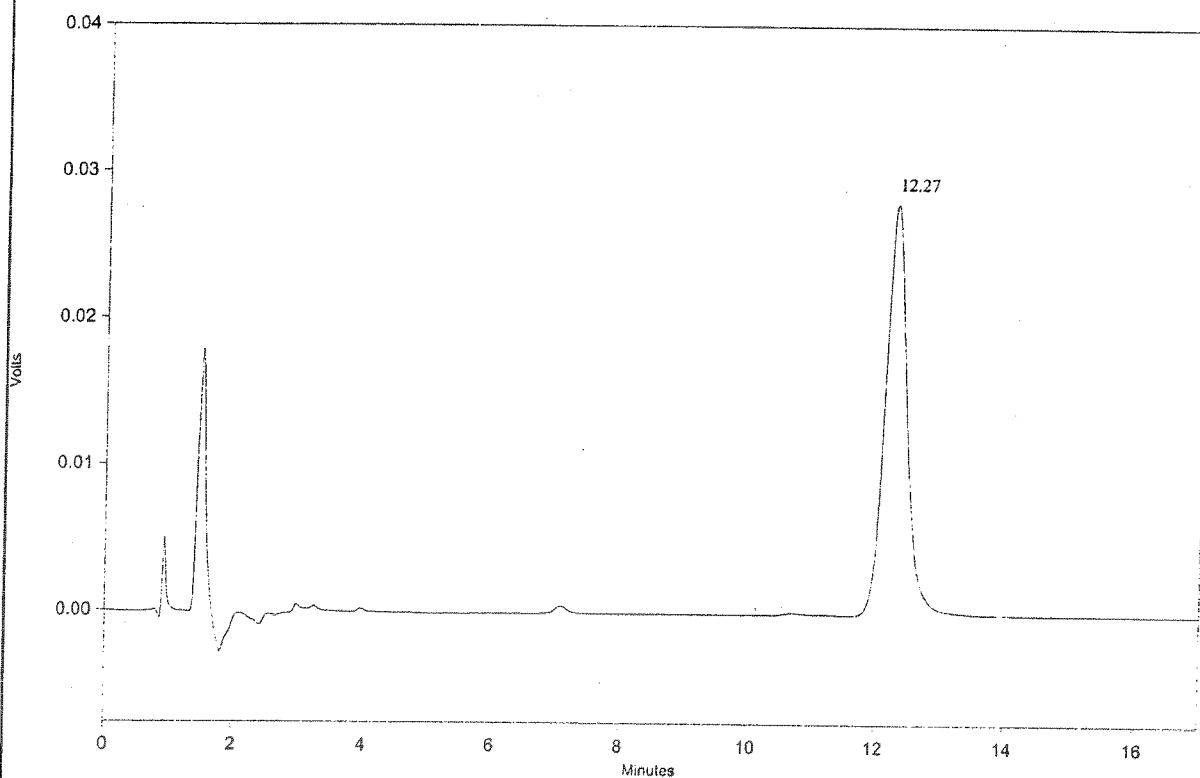
Vial: 2

Injection Volume: 50 ul

Detector A  
(218nm)

Pk #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates
1	Digoxin	12.27	681506	28038	1.2	0.0	6000

Totals			681506	28038			
--------	--	--	--------	-------	--	--	--



Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C

ATTACHMENT A - Page 5 of 20 pages

Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: Standard Solution 1 (CCV)

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\Std.Soln-Rep3

Date: 02/14/2008 8:52:52 AM

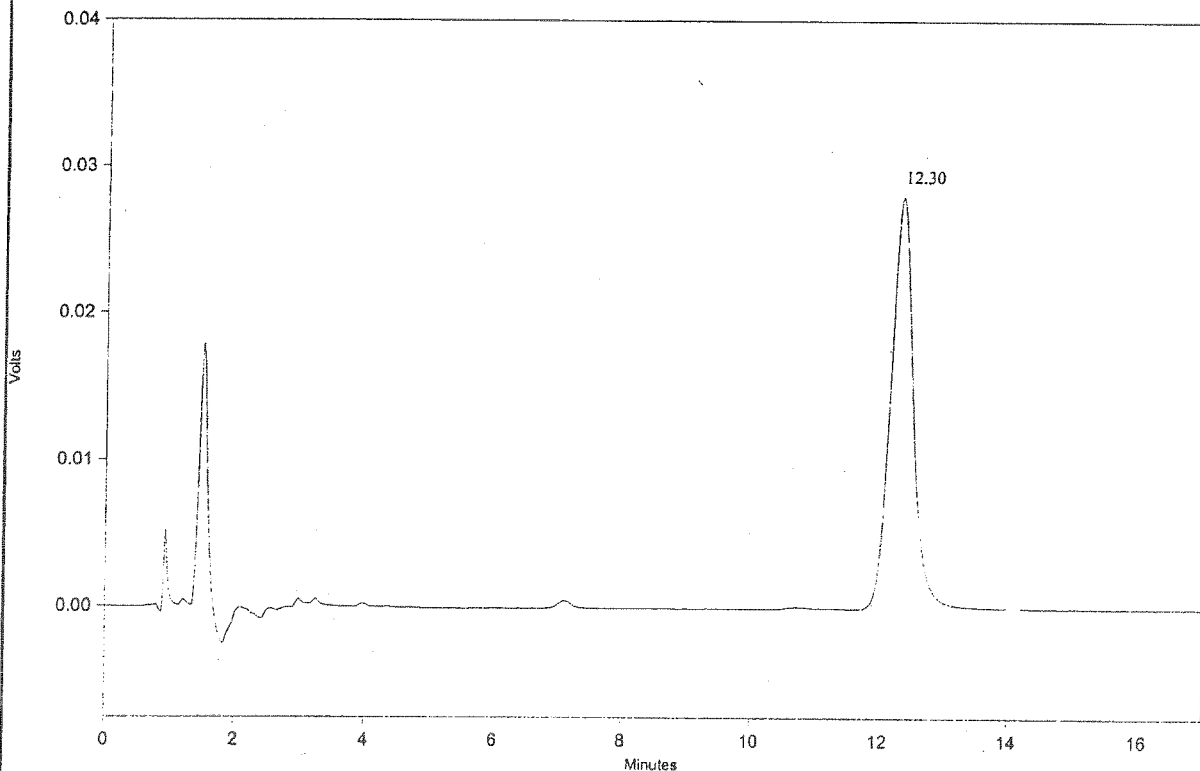
Vial: 2

Injection Volume: 50 ul

Detector A  
(218nm)

Pk #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates
1	Digoxin	12.30	683776	28055	1.2	0.0	5992

Totals			683776	28055			
--------	--	--	--------	-------	--	--	--



Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C

ATTACHMENT A - Page 6 of 20 pages

Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: Standard Solution 1 (CCV)

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\Std.Soln-Rep4

Date: 02/14/2008 9:11:15 AM

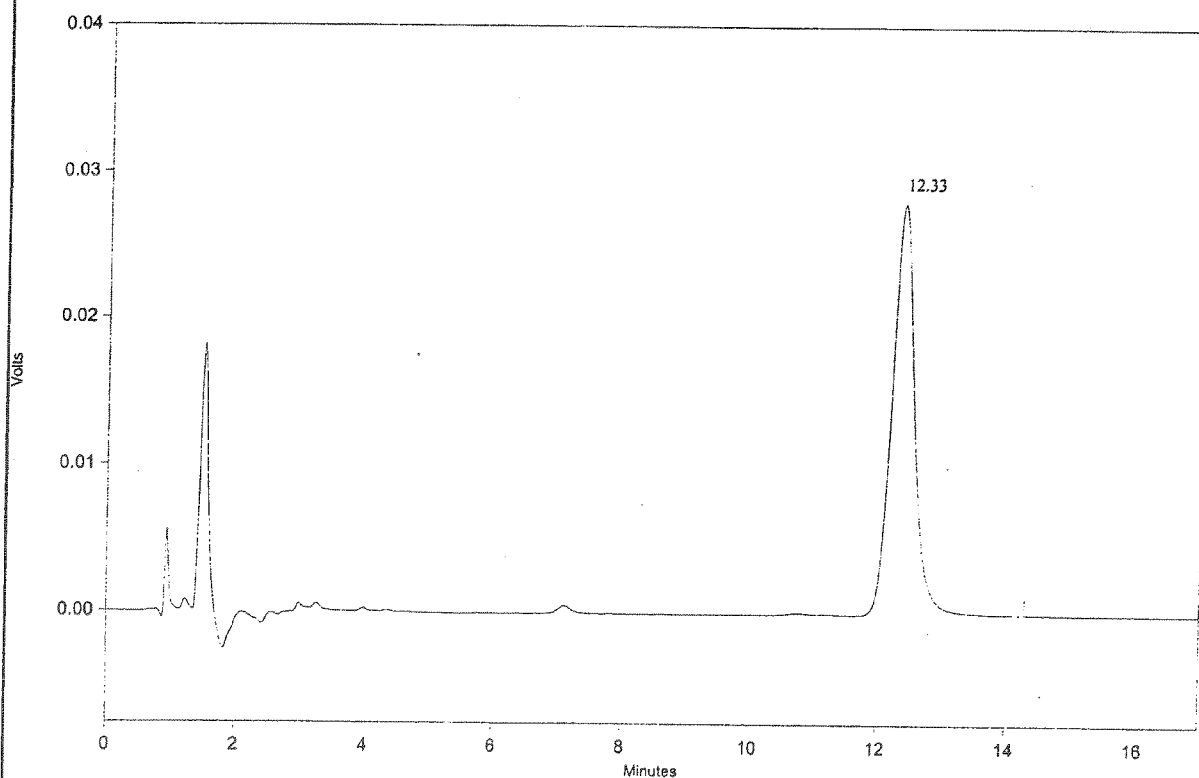
Vial: 2

Injection Volume: 50 ul

Detector A  
(218nm)

Pk #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates
1	Digoxin	12.33	684459	28000	1.2	0.0	6038

Totals			684459	28000			
--------	--	--	--------	-------	--	--	--



Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C

ATTACHMENT A - Page 7 of 20 pages

Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: Standard Solution 1 (CCV)

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\Std.Soln-Rep5

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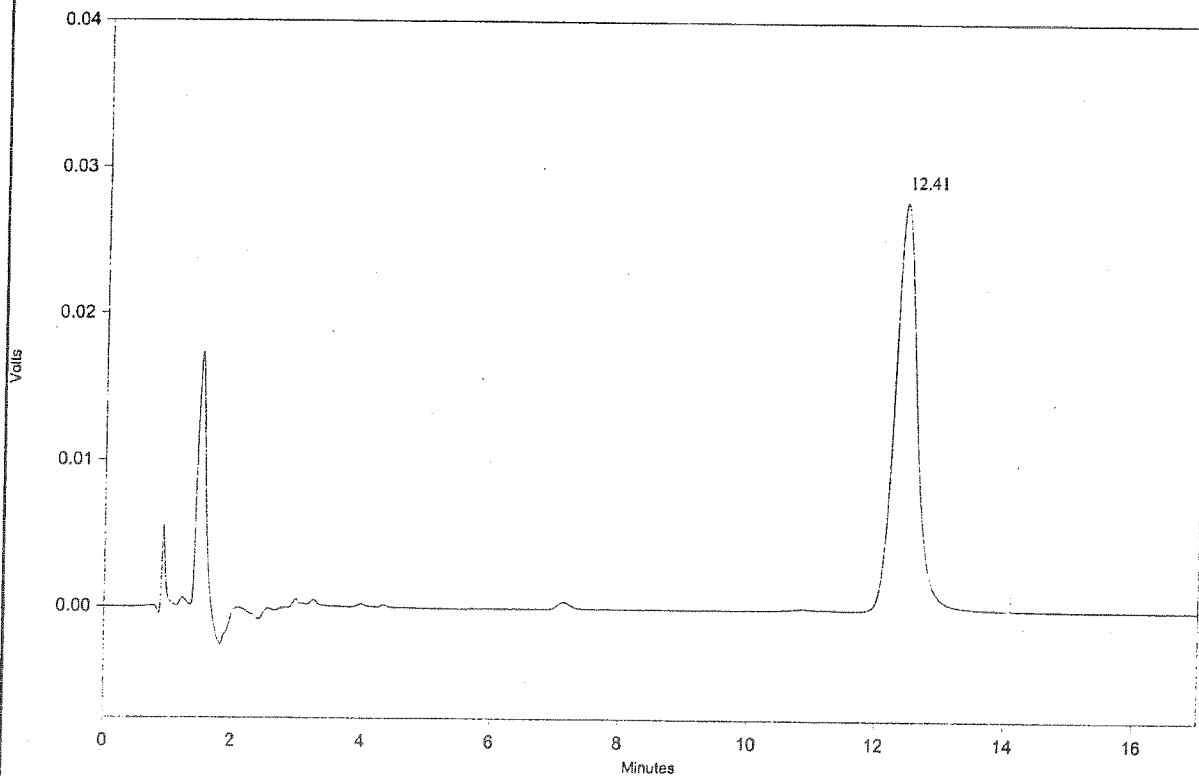
Vial: 2

Injection Volume: 50 ul

Detector A  
(218nm)

Pk #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates
1	Digoxin	12.41	680681	27850	1.2	0.0	6093

Totals			680681	27850			
--------	--	--	--------	-------	--	--	--



Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C



ATTACHMENT A - Page 8 of 20 pages

Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: Standard Solution 2 (ICV)

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\CheckStd.

Date: 02/14/2008 9:48:09 AM

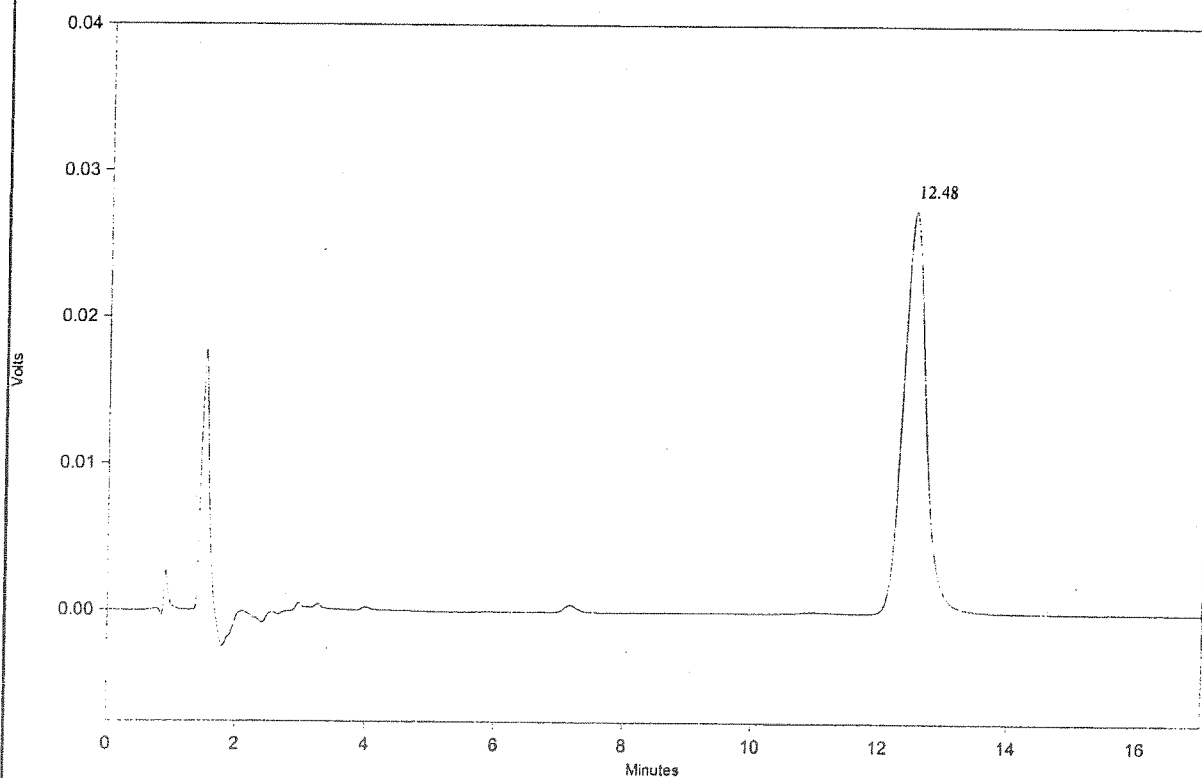
Vial: 3

Injection Volume: 50 ul

Detector A  
(218nm)

Pk #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates
1	Digoxin	12.48	673965	27423	1.2	0.0	6225

Totals			673965	27423			
--------	--	--	--------	-------	--	--	--



Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C

ATTACHMENT A - Page 9 of 20 pages

Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: Tablet 1

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\Tab1

Date: 02/14/2008 10:14:02 AM

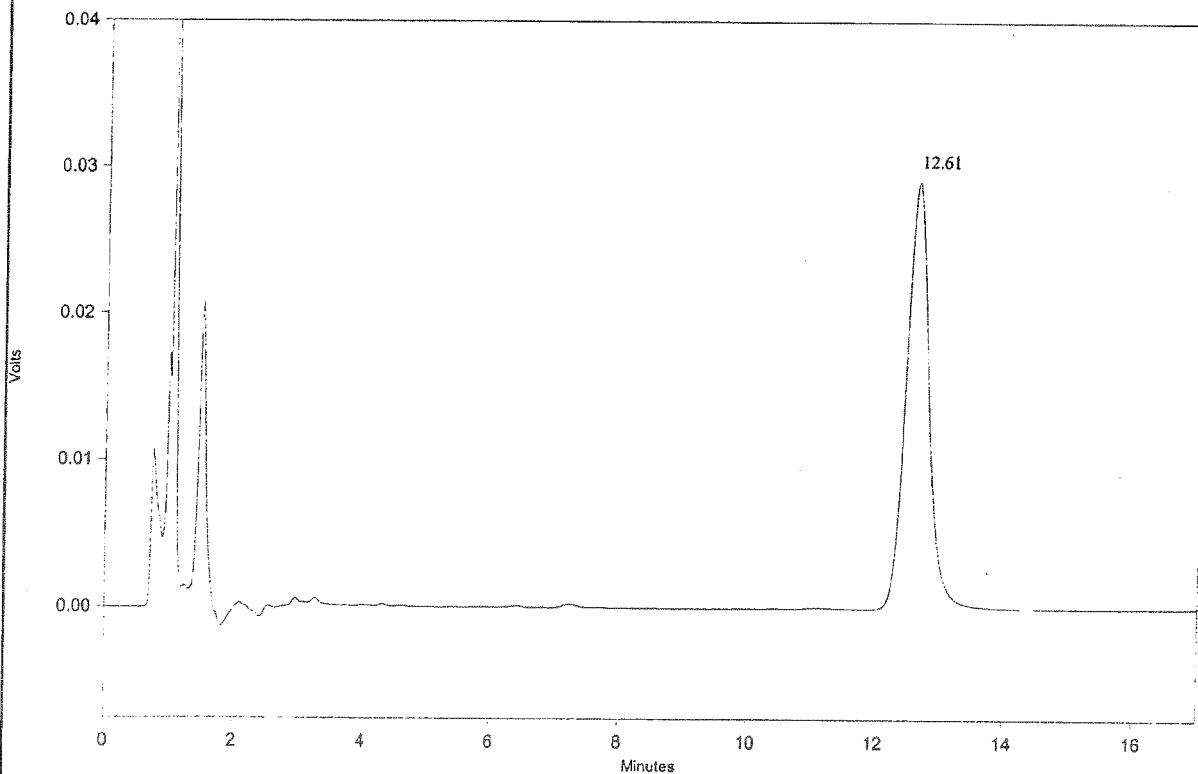
Vial: 4

Injection Volume: 50 ul

Detector A  
(218nm)

Pk #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates
1	Digoxin	12.61	713065	29069	1.2	0.0	6242

Totals			713065	29069			
--------	--	--	--------	-------	--	--	--



Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C

ATTACHMENT A - Page 10 of 20 pages

Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: Tablet 2

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\Tab2

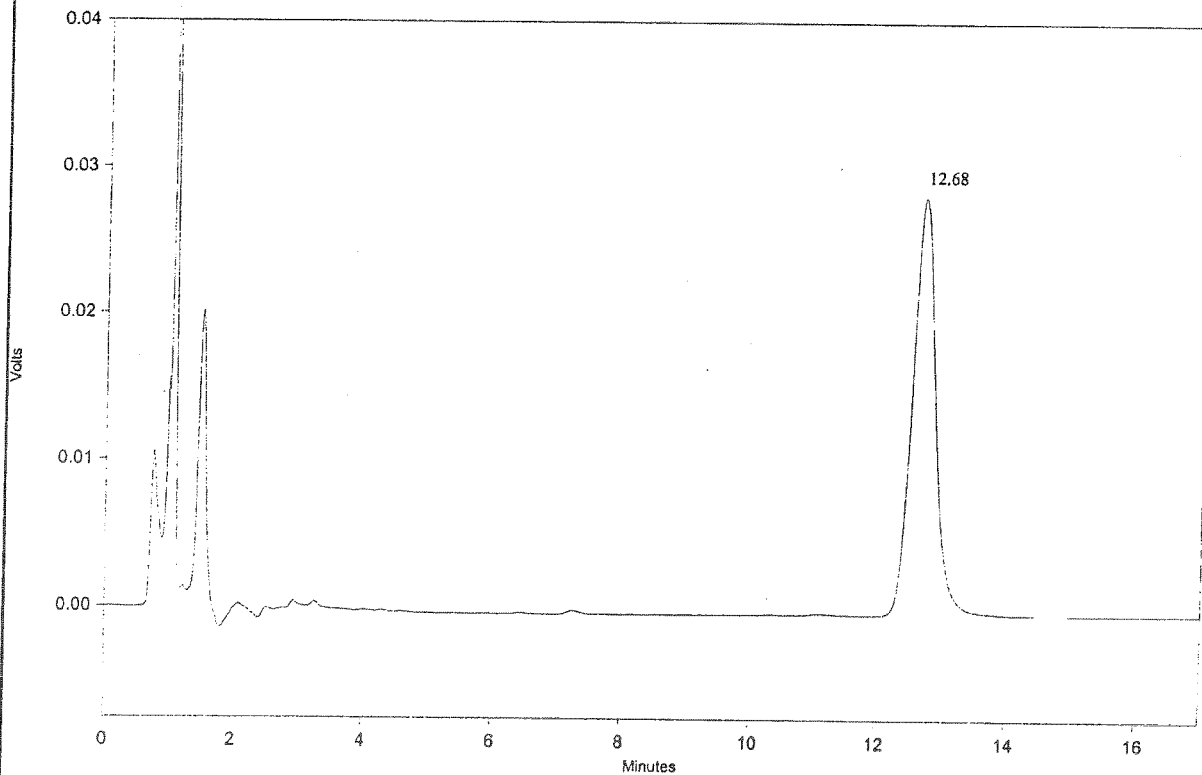
Date: 02/14/2008 10:34:52 AM

Vial: 5

Injection Volume: 50 ul

Detector A  
(218nm)

Pk #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates
1	Digoxin	12.68	702312	28498	1.2	0.0	6286
Totals			702312	28498			



Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C

ATTACHMENT A - Page 11 of 20 pages

Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: Tablet 3

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\Tab3

Date: 02/14/2008 10:53:43 AM

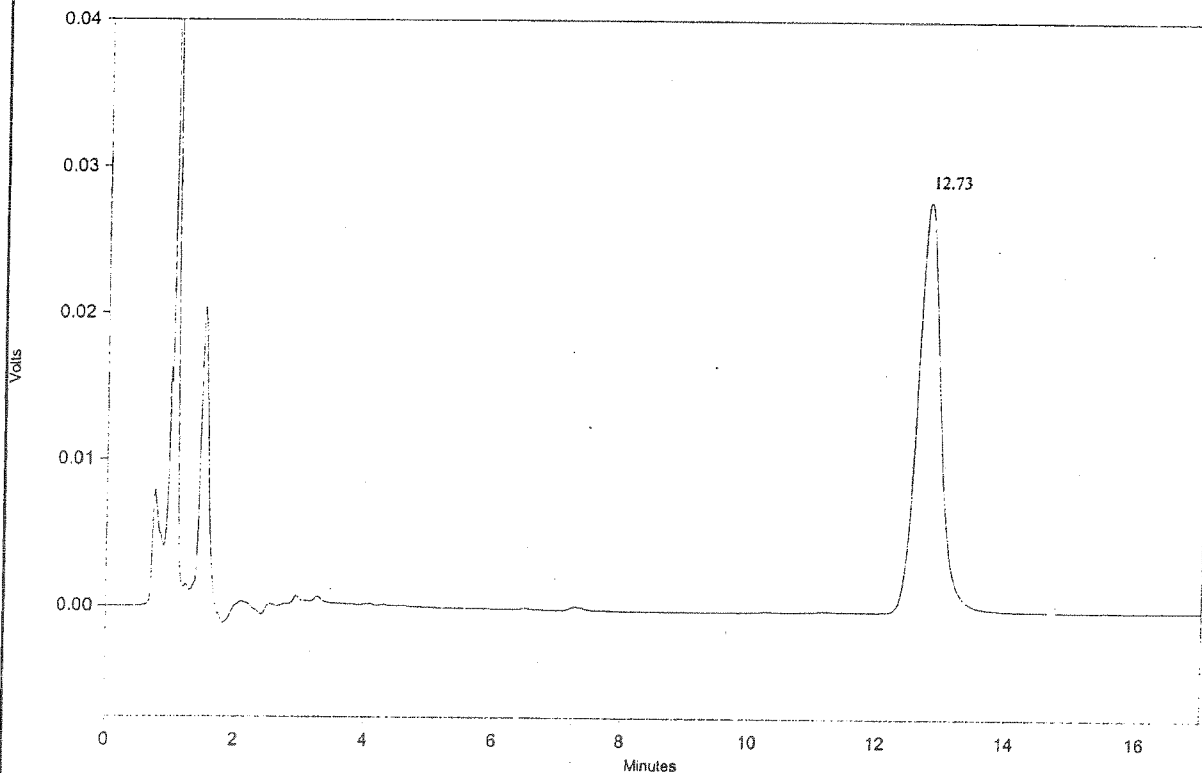
Vial: 6

Injection Volume: 50 ul

Detector A  
(218nm)

Pk #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates
1	Digoxin	12.73	695180	27999	1.2	0.0	6264

Totals			695180	27999			
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Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C

ATTACHMENT A - Page 62 of 20 pages

Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: Tablet 4

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\Tab4

Date: 02/14/2008 11:14:07 AM

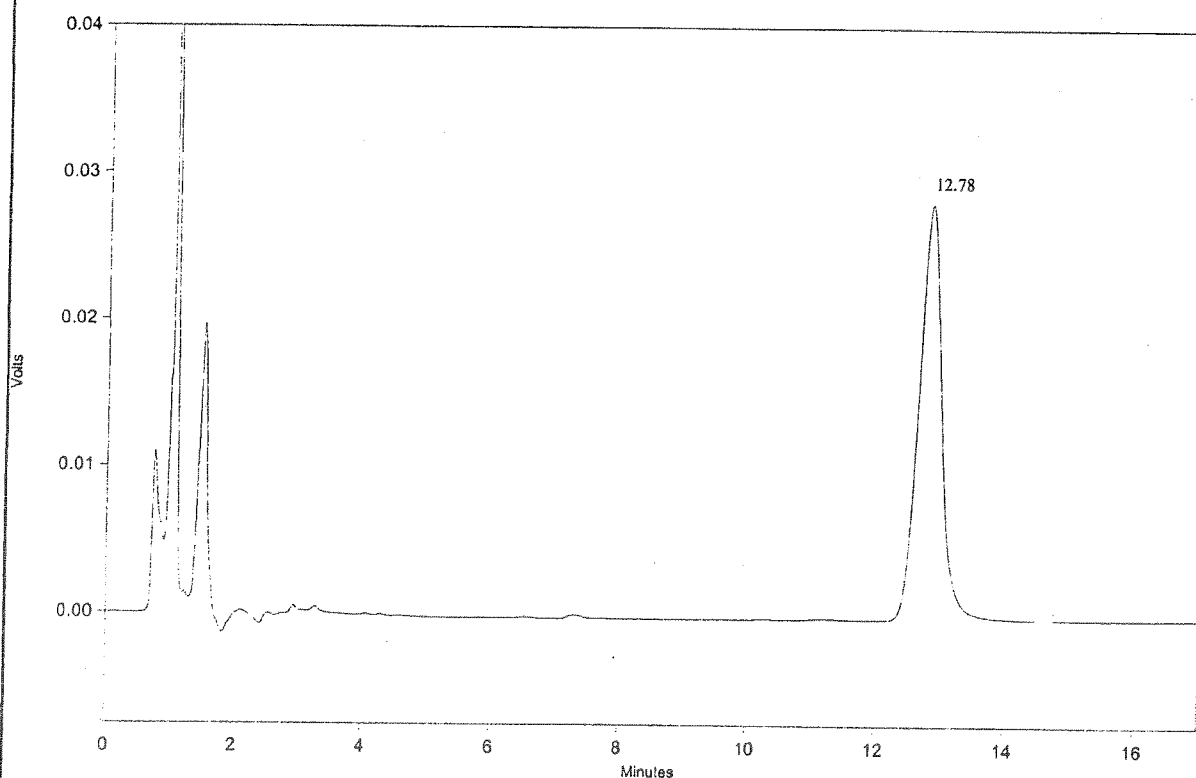
Vial: 7

Injection Volume: 50 ul

Detector A  
(218nm)

PK #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates
1	Digoxin	12.78	701285	28354	1.2	0.0	6357

Totals			701285	28354			
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Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C

ATTACHMENT A - Page 13 of 20 pages

Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: Tablet 5

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\Tab5

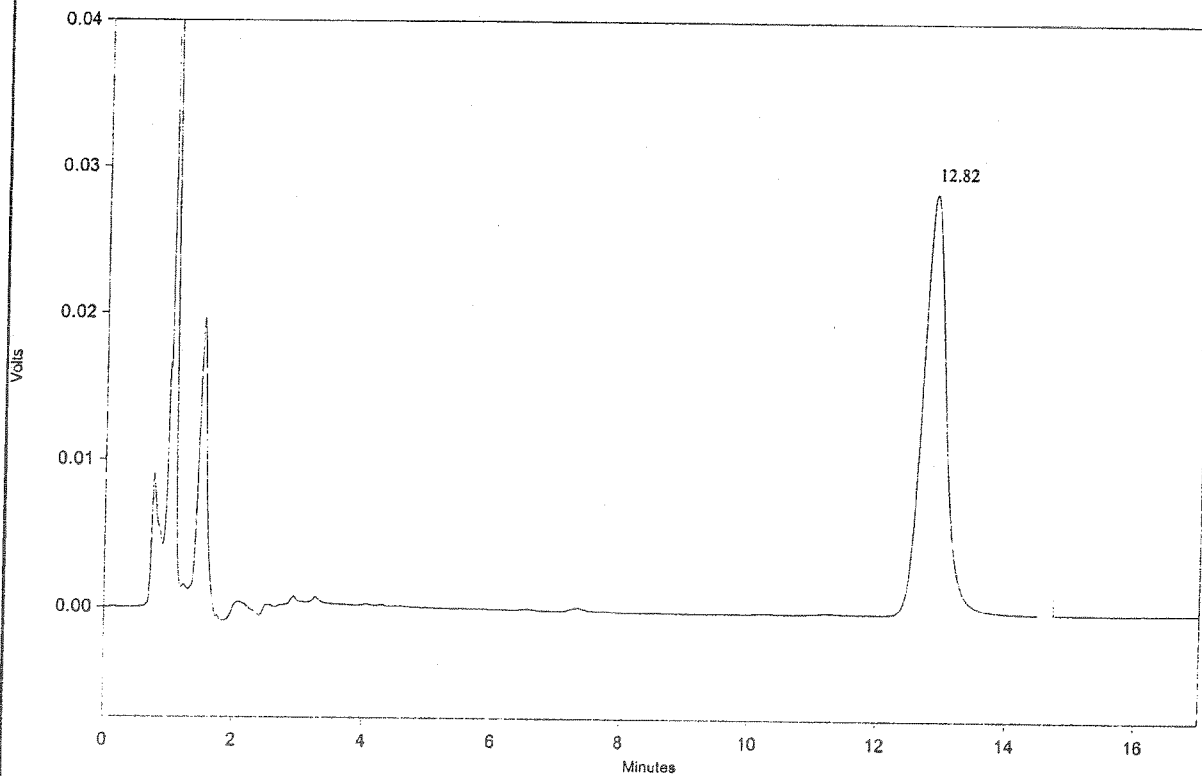
Date: 02/14/2008 11:32:37 AM

Vial: 8

Injection Volume: 50 ul

Detector A  
(218nm)

PK #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates
1	Digoxin	12.82	711091	28594	1.2	0.0	6403
Totals			711091	28594			



Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C

ATTACHMENT A - Page 14 of 20 pages

Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: Standard Solution 1 (CCV)

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\Std.Soln.6

Date: 02/14/2008 11:51:06 AM

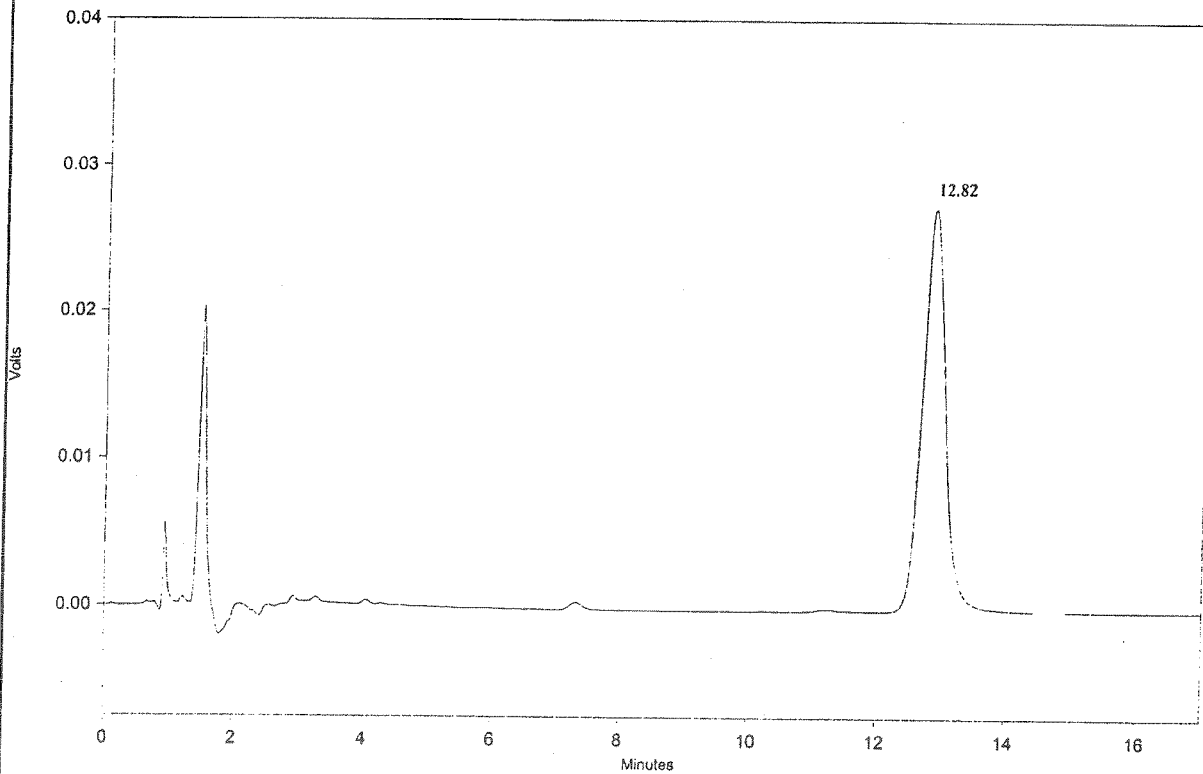
Vial: 2

Injection Volume: 50 ul

Detector A  
(218nm)

Pk #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates
1	Digoxin	12.82	679546	27412	1.2	0.0	6459

Totals			679546	27412			
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Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C



ATTACHMENT A - Page 15 of 20 pages

Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: Tablet 6

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\Tab6

Date: 02/14/2008 12:09:34 PM

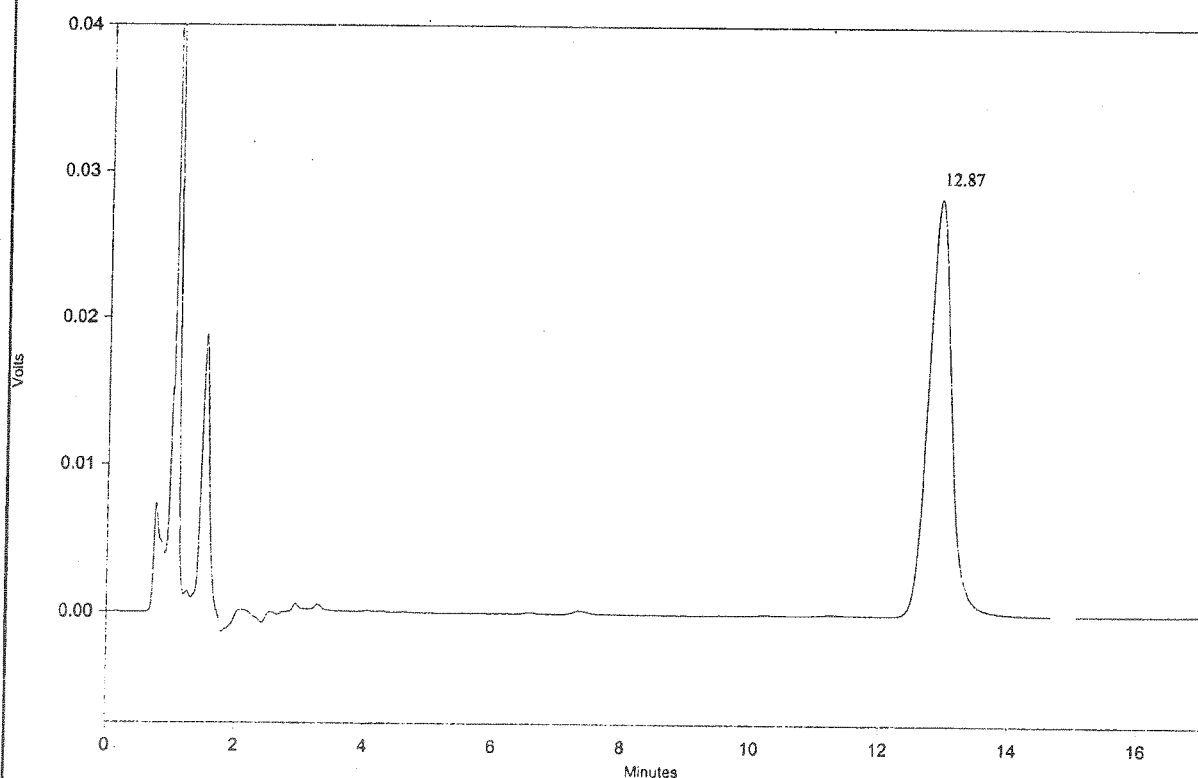
Vial: 9

Injection Volume: 50 ul

Detector A  
(218nm)

PK #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates
1	Digoxin	12.87	708580	28411	1.2	0.0	6289

Totals			708580	28411			
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Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C

ATTACHMENT A - Page 16 of 20 pages

Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: Tablet 7

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\Tab7

Date: 02/14/2008 12:28:03 PM

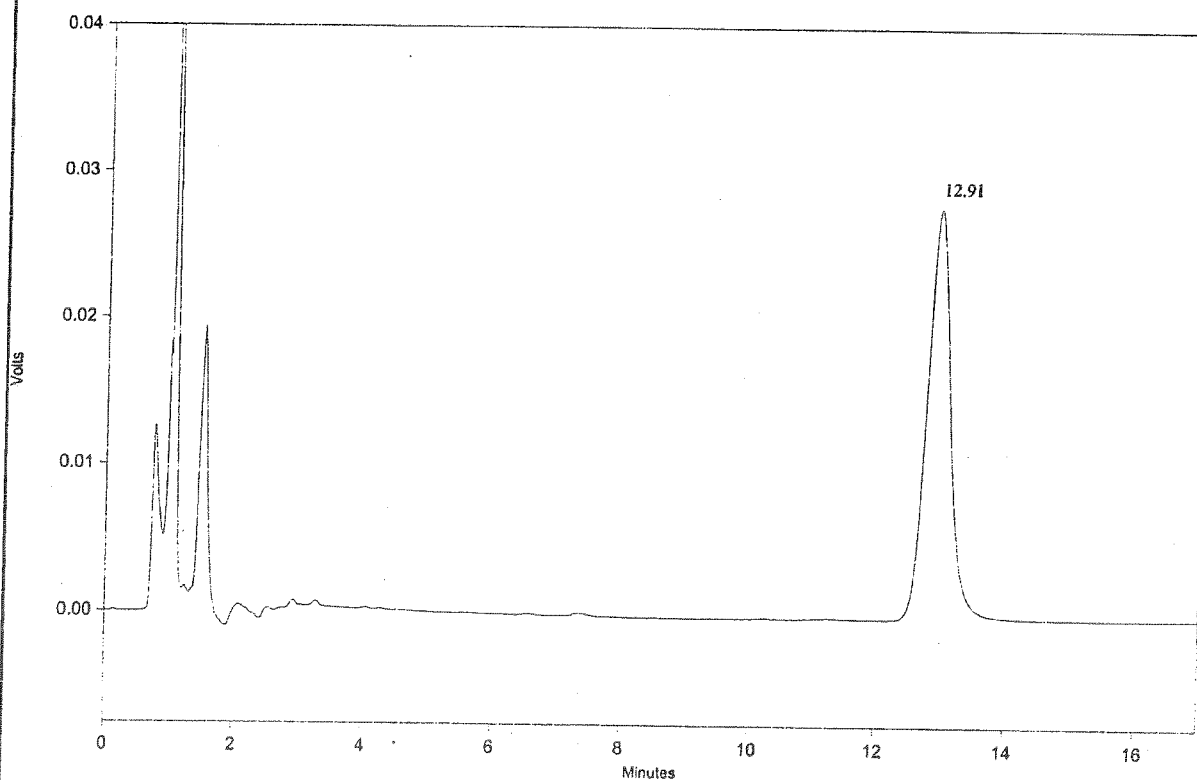
Vial: 10

Injection Volume: 50 ul

Detector A  
(218nm)

PK #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates
1	Digoxin	12.91	698918	27940	1.2	0.0	6319

Totals			698918	27940			
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Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C

ATTACHMENT A - Page 17 of 20 pages

Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: Tablet 8

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\Tab8

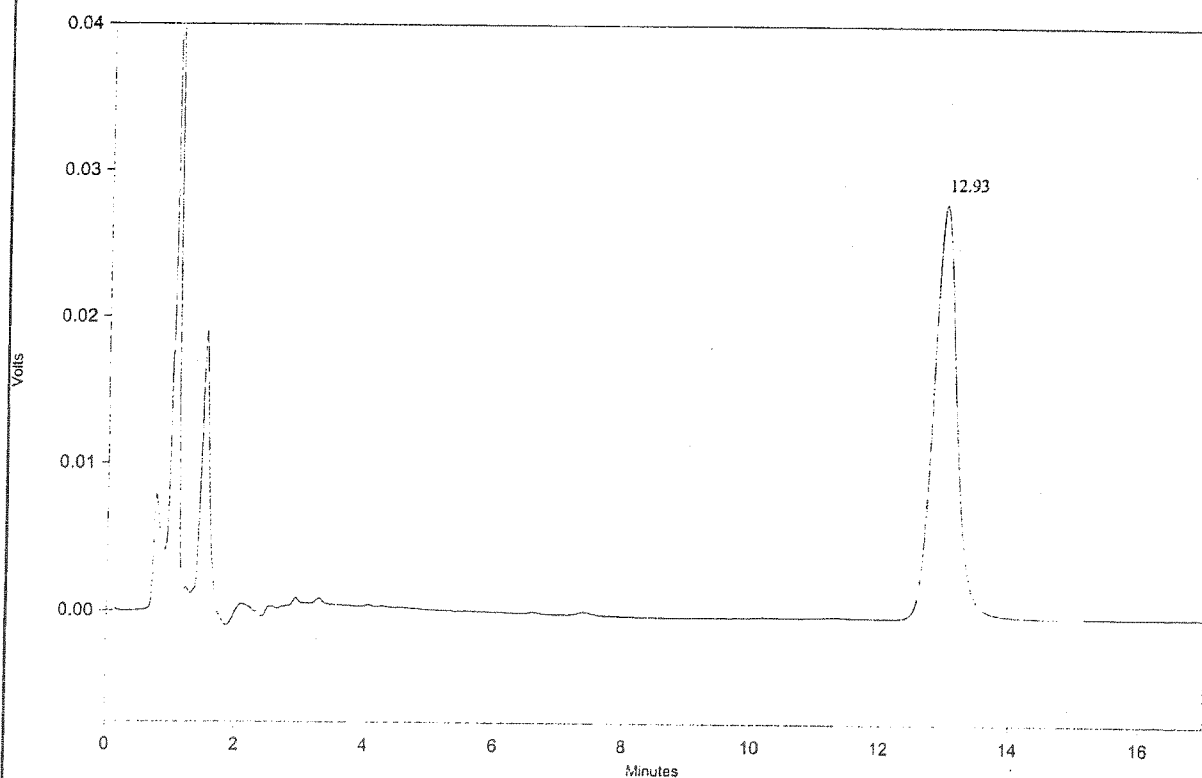
Date: 02/14/2008 12:46:31 PM

Vial: 11

Injection Volume: 50 ul

Detector A  
(218nm)

Pk #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates
1	Digoxin	12.93	707409	28170	1.1	0.0	6279
Totals			707409	28170			



Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C

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Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: Tablet 9

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\Tab9

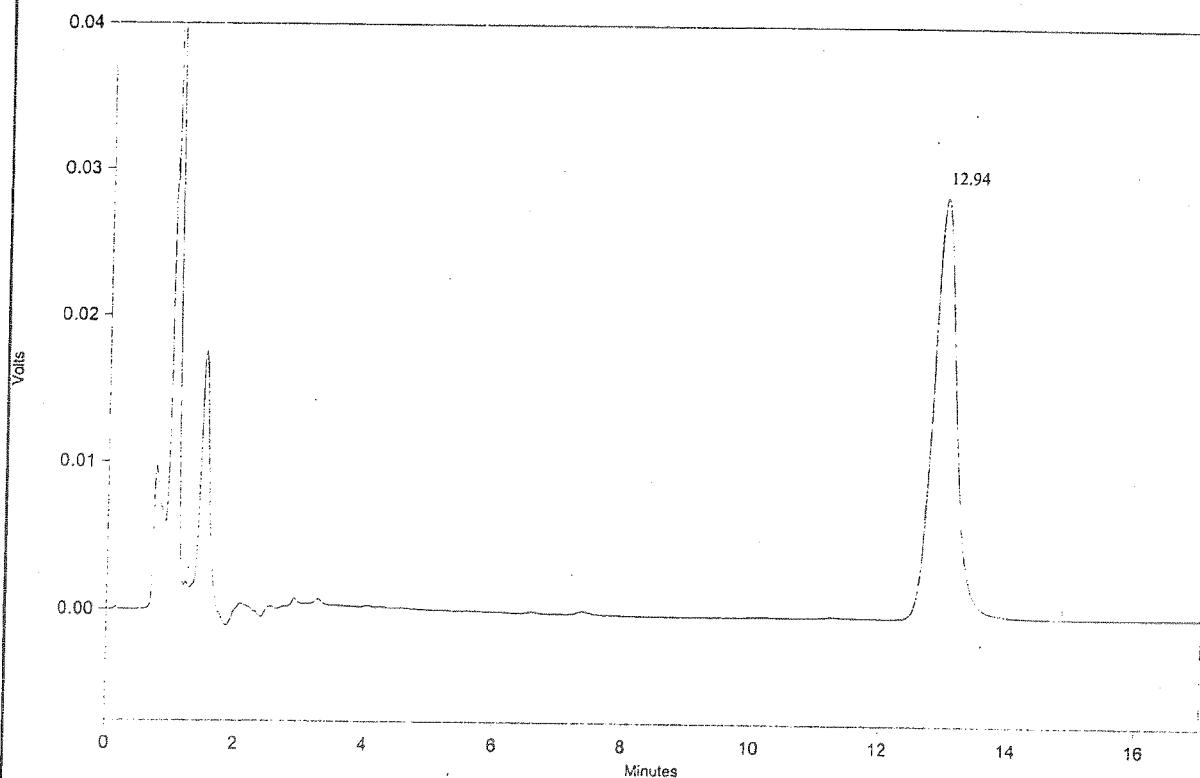
Date: 02/14/2008 1:04:59 PM

Vial: 12

Injection Volume: 50 ul

Detector A  
(218nm)

Pk #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates
1	Digoxin	12.94	718912	28615	1.1	0.0	6294
Totals			718912	28615			



Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C

ATTACHMENT A - Page 19 of 20 pages

Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: Tablet 10

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\Tab10

Date: 02/14/2008 1:23:28 PM

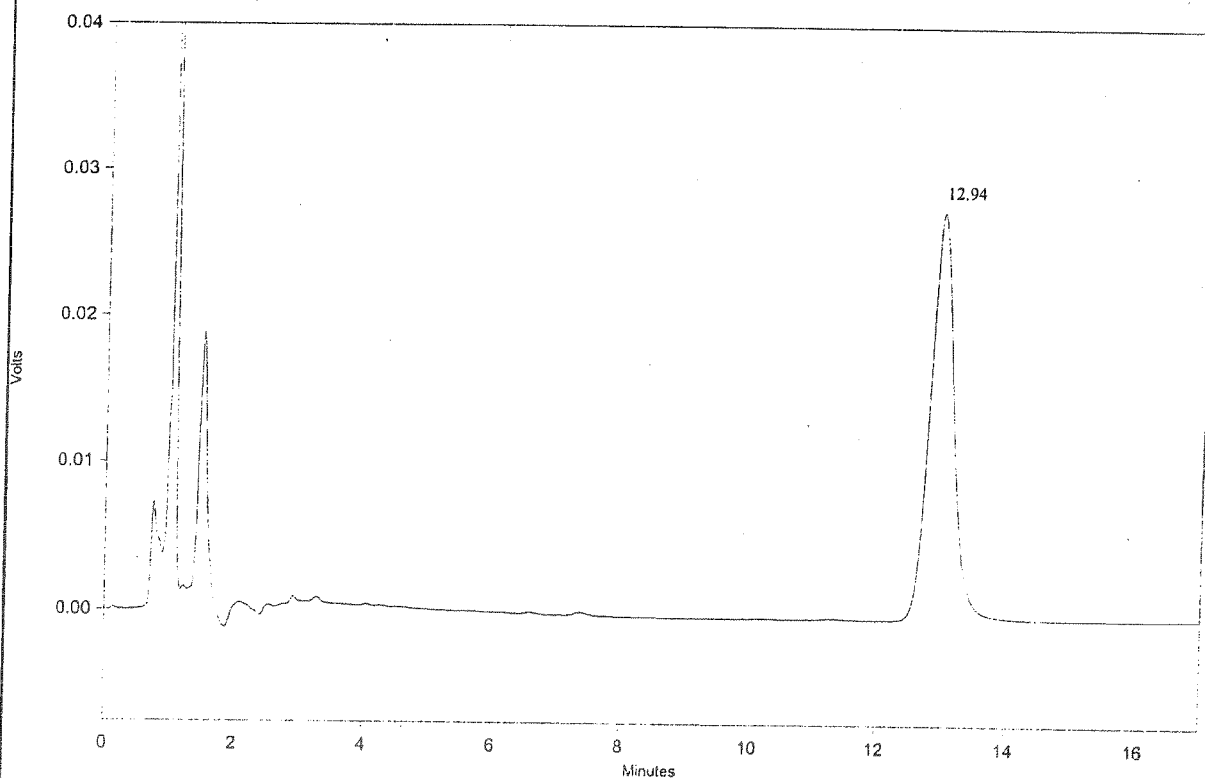
Vial: 13

Injection Volume: 50 ul

Detector A  
(218nm)

Pk #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates
1	Digoxin	12.94	695739	27693	1.2	0.0	6271

Totals			695739	27693			
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Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C

ATTACHMENT A - Page 20 of 20 pages

Product: Digoxin Tablets (0.125 mg)

Spl.No. 448881

Name: Standard Solution 1 (CCV)

Method: C:\CLASS-VP\METHODS\DigoxinTabs.met

File: C:\CLASS-VP\DATA\DigoxinTabs\448881\Std.Soln.7

Date: 02/14/2008 1:41:56 PM

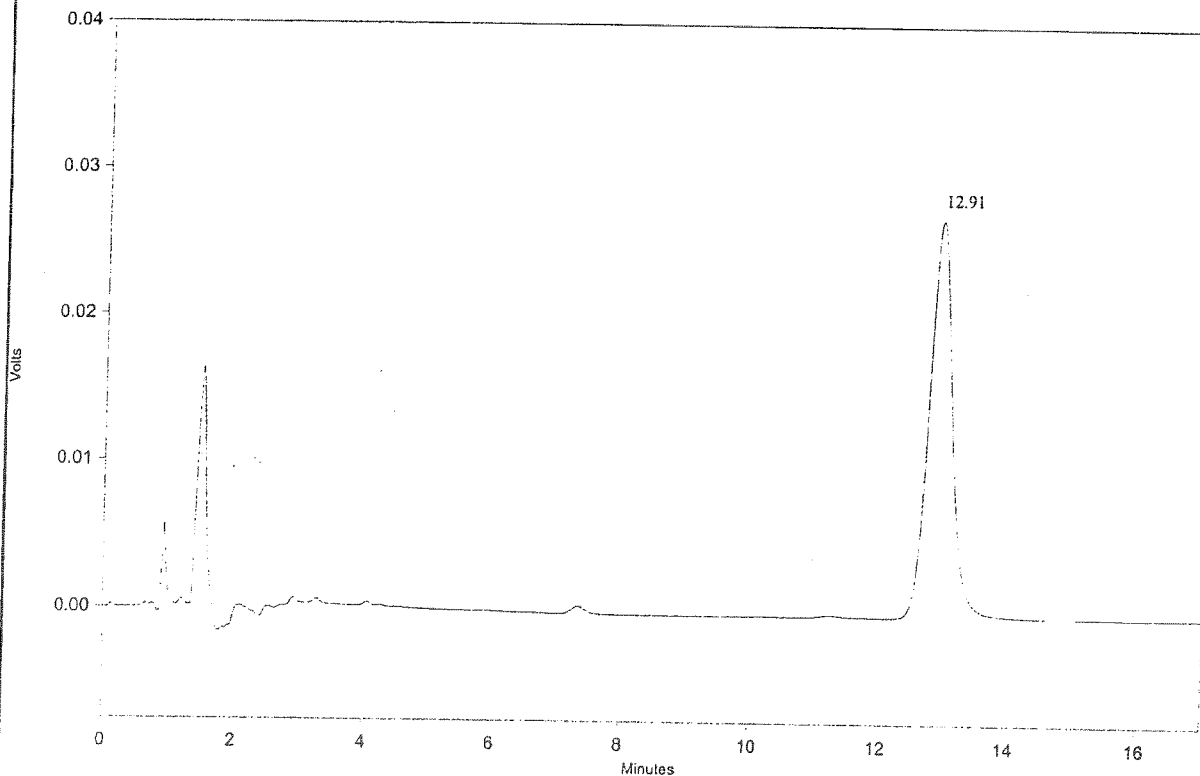
Vial: 2

Injection Volume: 50 ul

Detector A  
(218nm)

Pk #	Name	Retention Time	Area	Height	Asymmetry	Resolution	Theoretical plates
1	Digoxin	12.91	681835	27080	1.1	0.0	6231

Totals			681835	27080			
--------	--	--	--------	-------	--	--	--



Instrument: Shimadzu HPLC LC-10AT VP, FDA# 5083845 (QA by V.Fiorella on 1/3/08)

Analyst: Valentino Fiorella

Mobile Phase: Acetonitrile/Water (26/74)

Flow: 2.0 ml/min.

Column: Supelcosil LC-18-DB (250 mm x 4.6 mm; 5 um), Serial No. 88682C

Digoxin Tablets (0.125 mg)

Spl.# 448881

2/4/08

VF

Labeling

NDC 62794-145-01

**DIGITEL**

(digoxin tablets, USP)

125 mcg (0.125 mg)

100 TABLETS

Sample # 448881  
VF  
2/4/08  
121 3 107

mcg (0.125 mg)  
precautions,  
ackage insert.  
sistant  
USP.  
in a dry  
ot  
sehold

N 3 62794-145-01 6

Distributed by:  
BERTEK PHARMACEUTICALS INC.  
Sugar Land, TX 77478 USA

Manufactured by:  
AMIDE PHARMACEUTICAL, INC.  
101 East Main Street  
Little Falls, NJ 07424 USA

Control No.: 70298A1  
Exp. Date: APR 09

8064-01 RBK145A1

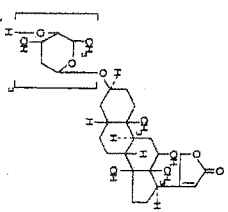
only



#448881  
2/4/08 VF



**DIGITEX<sup>®</sup>**  
(digoxin tablets, USP)



Diglycom is described chemically as (3 R, 5 R, 12 R)-3-(0-2,6-dideoxy- $\beta$ -D-ribo-hexapranosyl-(1 $\rightarrow$ 4)-0-2,6-dideoxy- $\beta$ -D-ribo-hexapranosyl-(1 $\rightarrow$ 4))-2,6-dideoxy- $\beta$ -D-ribo-hexapranosyl-(1 $\rightarrow$ 2)-1,2,3,4,6-pentaoxy- $\alpha$ -D-20(22)-enitol. Its molecular formula is  $C_{44}H_{80}O_{21}$ . Its molecular weight is 780.94, and the structural formula shown.

Biguanin salts as odorless white crystals that melt with decomposition above 230°C. The drug is practically insoluble in water and is either slightly soluble in diluted (50%) alcohol and in chloroform, and freely soluble in pyridine.

DIBETEX is supplied as 125-mg (0.125-mg) or 250-mg (0.25-mg) tablets for oral administration. Each tablet contains the labelled amount of dipeptidyl DCP and the following inactive ingredients: corn starch, croscarmellose sodium, microcrystalline cellulose, pregelatinized starch, lactose monohydrate and anhydrous lactose, silicon dioxide and stearic acid. In addition, the 125-mg (0.125-mg) tablets contain DSC Yellow No. 10 Aluminium Lake.

depressant system mediated by effects on the autonomic nervous system. The autonomic nervous system is a complex system that controls the body's internal organs and functions. It is divided into the sympathetic and parasympathetic systems. The sympathetic system is responsible for the 'fight or flight' response, while the parasympathetic system is responsible for the 'rest and digest' response. The autonomic nervous system is controlled by the brain and spinal cord. It is a complex system that controls the body's internal organs and functions. It is divided into the sympathetic and parasympathetic systems. The sympathetic system is responsible for the 'fight or flight' response, while the parasympathetic system is responsible for the 'rest and digest' response. The autonomic nervous system is controlled by the brain and spinal cord.

[illegible]

(2) a decrease in the degree of activation of the sympathetic nervous system; and (3) slowing of the heart rate and decreased conduction velocity through the AV node (vagal/parasympathetic effect). The effects of ligand withdrawal on the AV node (vagal/parasympathetic effect) in a rabbit failure are mediated by its positive inotropic and neurotropic (enhancing effects), whereas the effects of the drug in atrial fibrillation are related to its vagomimetic actions. In high doses, the drug increases vagomimetic outflow from the central nervous system.

**Pharmacokinetics: Absorption.** Following oral administration, peak serum concentrations of digoxin occur at 1 to 2 hours. Absorption of digoxin from digoxin tablets has been demonstrated to be 60% to 80%, complete compared to an identical intravenous dose of digoxin (105). This increase in sympathetic activity may be an important factor in digoxin toxicity.

**Table 1: Comparisons of the Systemic Availability and Equivalent Doses for Oral Preparations of Meprobamate**

Product	Assayable Bio-availability	Equivalent Dosing <sup>a</sup> Average Doses for Forms
Diphen Tablets	80-85%	125 250 500
Diphen Product Elute	70-85%	62.5 125 250 500
Diphen Solution		50 100 200 400
Diphen Capsules	90-100%	50 100 200 400
Diphen Injection/V	100%	50 100 200 400

\*For example, 125-mcg Digoxin tablets equivalent to 125 mcg Digoxin Pediatric Eladr equivalent to 100 mcg Digoxin Solution in Capsules equivalent to 100 mcg Digoxin Injectively.

the induction products (e.g., fibrinogen) by coagulase bacteria in the gut. Data suggest that one in ten patients treated with digoxin tablets will degrade 40% or more of the ingested dose as a result of certain antibiotics may increase the absorption of digoxin in such patients. Although inactivation of these bacteria by antibiotics is rapid, the serum digoxin concentration will rise at a rate consistent with the elimination half-life of digoxin, the magnitude of rise in serum digoxin concentration relates to the extent of bacterial inactivation, and may be as much as two-fold in some cases.

[illegible]

Diphenyl concentrated in tissues and therefore has a large apparent volume of distribution. Uptake crosses with the blood-brain barrier and the placenta. At delivery, the serum diphenyl concentration in the neonate is similar to the serum concentration in the mother. Approximately 25% of diphenyl in the placenta is bound to protein. Serum diphenyl concentrations are not significantly altered by large doses of phenytoin, so that it remains a useful serum correlate for assessing drug levels. Diphenyl has a half-life of 20–40 h and low weight.

As with many (i.e., many) antiepileptics, 15% of a dose of diphenyl is metabolized. The metabolites, 5-phenyl-2-methyl-3-pyridinecarboxamide and 5-phenyl-2-methyl-3-pyridinecarboxylic acid, are 3- and 4-fold different, and their pharmacokinetic and anticonvulsant potencies are similar. The metabolites are excreted in urine, and the parent is excreted in urine and is also excreted in breast milk. The metabolites of diphenyl are not dependent upon the cytochrome P-450 system, and diphenyl is not known to induce or inhibit the cytochrome P-450 system.

**Excretion.** Elimination of digoxin follows first-order kinetics (that is, the quantity of digoxin eliminated at any time is proportional to the total body content). Following intravenous administration to healthy volunteers, 50% to 70% of a digoxin dose is excreted unchanged in the urine. Renal excretion of digoxin is proportional to healthy glomerular filtration rate and is largely independent of urine flow. In healthy volunteers with normal renal function, digoxin has a half-life of 1.5 to 2 days. The half-life in patients with congestive heart failure is 1.5 to 3 days. Digoxin is not effectively removed from the body by dialysis, exchange transfusion, or extracorporeal membrane oxygenation. Because most of the drug is bound to tissue and does not circulate in the blood,

**Special Populations:** Race differences in digoxin pharmacokinetics have not been formally studied. Because digoxin is primarily eliminated as unchanged drug via the kidney and because there are no important differences in creatinine clearance among races, pharmacokinetic differences due to race are not expected.

The clearance of digoxin can be primarily controlled with renal function as indicated by creatinine clearance. The Doxerent and Doxent formulas for estimation of creatinine clearance involves age, body weight, and gender. A table that provides the usual daily maintenance dose requirements of digoxin tablets based on creatinine clearance (see 70 k2) is presented in the DOXAGE AND ADMINISTRATION section.

Patients requiring concentration therapies in patients with acid hyperkalemia generally fall within the range of profiles in a group of healthy subjects.

Product	Time to Onset of Effect*	Time to Peak Effect*
Diphenhydramine	0.5-2 hours	2-6 hours
Diphenhydramine Elixir	0.5-2 hours	2-6 hours
Diphenhydramine Syringe	0.5-2 hours	2-6 hours
Carisoprodol	5-30 minutes†	1-4 hours

cardiac effects and electrocardiographic changes, depending upon rate of infusion.

**Concise Heart Failure.** Two 12-week, double-blind, placebo-controlled studies enrolled 178 (RADIANCE trial) and 86 (PROVED trial) patients with NYHA class I or II heart failure previously treated with angiotensin converting enzyme inhibitors. In both studies, treatment with sacubitril/valsartan (200/80 mg b.i.d.) significantly reduced the risk of cardiovascular death, hospitalization for heart failure, and an ACE inhibitor (RADIANCE only) and treatment with sacubitril/valsartan (50/80 mg b.i.d.) significantly reduced the risk of death or hospitalization for heart failure compared with treatment with enalapril (20 mg b.i.d.).

The Oxyphils Investment Group (OIG) main trial was a multi-centre, randomised, double-blind, placebo-controlled mainly study of 1545 patients with heart failure and left ventricular ejection fraction  $\leq 45\%$ . At inclusion, 67% were NYctAS and 11.1% had heart failure of ischaemic aetiology. 44% had been previously diagnosed and treated with diuretics, 44% had been receiving digoxin, and 20% were non-compliant. ACE inhibitors,  $\beta$ -blockers, and aspirin were given to all patients. The trial was terminated early because of the results in the placebo arm, where there was a trend to treatment benefit.

[illegible]

PAIN UNIT	n	Risk of All-Cause Mortality or All-Cause Hospitalization*		Relative risk†
		Fentanyl	Trigeminal	
1000 patients	5802	524	553	0.94 (0.86, 1.03)
1000 AM	549	541		0.96 (0.83, 1.04)

F 0.25-0.45	4543	568	571	0.99 (0.91-1.07)
IR ≤ 0.55	4455	561	563	0.98 (0.91-1.06)
				0.88

RM (RMV)	F < 0.25	IR > 0.25	F > 0.45*
2224	2258	2346	987
719	677	687	571
696	637	650	585
(0.80-0.97) 0.84	(0.76-0.93) 0.85	(0.77-0.94)	1.04 (0.88-1.23)

N	Risk of a 10% reduction in 1st Cause hospitalization		
	Pharmco	Diogen	Relative risk <sup>a</sup>
5882	524	533	0.94
4571	549	571	0.96
4543	568	541	0.89 (1.04)
4455	561	563	0.98
2224	719	696	0.88 (0.87)
2258	677	637	0.84
2346	627	630	0.76 (0.93)
587	571	585	0.77 (0.86)
			1.04
			(0.89-1.23)

pH	Free Protein ( $\bar{p}I = 0.55$ )	Risk of Severe Metabolic or Electrolyte Imbalances	
		Protono	Diogeno
7.35-7.45	5681	294	0.63 (n 53.0/76)
7.25-7.35	4571	242	0.70 (n 52.0/80)
7.15-7.25	4543	244	0.74 (n 54.0/84)

	Prevalence	Specificity	Sensitivity	PPV	NPV	LR+	LR-
CF < 0.45	0.001	0.954	0.217	0.001	0.954	0.001	0.954
CF 0.45-0.65	0.453	0.242	0.175	0.453	0.242	0.453	0.242
CF > 0.65	0.545	0.244	0.180	0.545	0.244	0.545	0.244
CF < 0.45	0.001	0.954	0.217	0.001	0.954	0.001	0.954
CF 0.45-0.65	0.453	0.242	0.175	0.453	0.242	0.453	0.242
CF > 0.65	0.545	0.244	0.180	0.545	0.244	0.545	0.244

Number of patients with an event during the first 2 years per 100 randomized patients.  
Relative risk (95% confidence interval).

In this secondary study, the results are consistent with the findings of the primary study. In structures where there is no statistically significant benefit from treatment, evidence from a trial's primary endpoint, results pertaining to secondary end-points should be interpreted cautiously. **Strategic Medical Decision Making** In patients with chronic atrial fibrillation, if you assess your patient's individual response rate in these doses of digoxin from 0.25 to 0.75 mg/day, digoxin should not be used for the treatment of multichannel atrial tachycardia.

**Pharmacokinetics** LAH is absorbed rapidly and completely. The half-life of LAH is 1.5 to 2.5 hours. LAH is excreted in the urine. The half-life of LAH is 1.5 to 2.5 hours. LAH is excreted in the urine.

**Pharmacodynamics** LAH is indicated for the treatment of atrial tachycardia.

**Central Paradox:** OTCX is indicated for the control of ventricular arrhythmias in patients with congestive heart failure. However, the drug is also known to be arrhythmogenic in patients with ventricular fibrillation or in patients with a known propensity for a arrhythmia. A susceptibility reaction to other digoxin preparations usually constitutes a contraindication to digoxin.

[illegible]

in Patients with Impaired Renal Function: Digenin is primarily excreted in the urine, and therefore, patients with impaired renal function may be at an increased risk of developing adverse effects. In patients with impaired renal function, the following precautions should be taken:

- **Monitoring:** Patients with impaired renal function should be monitored closely for signs and symptoms of adverse effects, such as dizziness, headache, and changes in vision.
- **Dose Adjustment:** The dose of Digenin should be adjusted based on the patient's renal function. Patients with severe renal impairment (creatinine clearance < 30 mL/min) should receive a lower dose than patients with normal renal function.
- **Contraindications:** Digenin should not be used in patients with severe renal impairment (creatinine clearance < 30 mL/min) or in patients with a history of severe allergic reactions to any of the ingredients of the drug.

Patients with impaired renal function should be advised to avoid alcohol and other substances that may interact with Digenin. Patients should also be advised to avoid driving or operating machinery while taking Digenin, as it may cause dizziness or blurred vision.

steady-state serum concentration in patients with renal impairment, a longer period of time is required to achieve an initial dose.

not taken to reduce the dose of digoxin, such patients are at high risk for toxicity and toxic effects will last longer in such patients than in patients with normal renal function.

muscular depletion sensitizes the myocardium to ethanol. This is desirable to maintain normal serum potassium and magnesium concentrations in patients being treated with diuretic drugs. These electrolytes may result from malnutrition, diarrhea, alcohol withdrawal, as well as the use of the following stress diuretics: furosemide, amiloride, H<sub>2</sub>O, carbonic anhydrase, and mechanical suction of gastrointestinal secretions.

Hypocalcemia from any cause predisposes the patient to

is sensory, cardiac, particularly when atrial fibrillation is present, may produce serious arrhythmias, in a dog subjected. On the other hand, hypocalcaemia can nullify the diagenic in humans; thus, diagen may be ineffective until serum is returned to normal. These interactions are related to the different effects conductivity and excitability of the heart similar to that of calcium.

Use in Human Beings and Pharmacokinetics. Studies have not traced the requirements for diagen. Heart failure and arrhythmias resulting from hypomagnesaemia of hypomagnesaemia (e.g., hypothyroidism, hypoparathyroidism) may be of aid in addressing the underlying condition. Adult patients with hypomagnesaemia states are particularly resistant to

Nevertheless, there must be access to several options if digoxin is used as a *Poisoned with Acute Mechanical Intoxication* of digoxin is used with caution in patients with acute myocardial infarction use of inotropic drugs in some patients in this setting may undesirable increases in myocardial oxygen demand and increase basal heart electrical conduction. It may be desirable to the dose of digoxin for 1 to 2 days prior to electrical cardioversion fibrillation to avoid the induction of ventricular arrhythmia. Physicians must consider the consequences of increased ventricular response if digoxin is withdrawn, if difficulty is

**Abstract** *Fast forwarding* (pretrial activity) signals the onset of sensory processing and is a critical component of the sensory system. However, the neural mechanisms underlying this activity are poorly understood. We used a combination of electrophysiological and imaging techniques to study the neural mechanisms underlying fast forwarding in the visual system. We found that fast forwarding is a result of a combination of factors, including the timing of the sensory input, the timing of the sensory processing, and the timing of the sensory output. We also found that fast forwarding is a result of a combination of factors, including the timing of the sensory input, the timing of the sensory processing, and the timing of the sensory output.

[illegible]

use of aqeous and suppositories increases the risk of anaphylaxis. *Streptococcus* may cause a sudden outbreak of skin from muscle cells, and may thereby cause anaphylaxis in test subjects. Although beta-adrenergic blockade with blockers and epinephrine may be useful in combination to control the reaction, their additive effects on  $\text{AT}$  node conduction can result in a complete heart block.

**Drug/Laboratory Test Interactions:** The use of therapeutic digoxin may cause prolongation of the PR interval and depress the ST segment on the electrocardiogram. Digoxin may produce a false ST-T change on the electrocardiogram as a side effect.

**Contraindications, Warnings, and Precautions:** There have been no long-term studies performed in animals to evaluate a genetic potential, nor have studies been conducted to assess the genetic potential of digoxin or its potential to affect fertility.

**Pregnancy, Fertility, and Lactation:** **Effects:** Pregnancy Category C.



**Effect:** Potential to affect fertility.

patients may have worsening of the outflow obstruction due to the side effects of digoxin.

**ADVERSE EFFECTS:**

**Arrhythmias with Impaired Atrial Function:** Digoxin is primarily used with the inotropes; therefore, patients with impaired renal function and congestive heart failure are at high risk for arrhythmias. Maintenance doses of digoxin (see **USE AND ADMINISTRATION**) are based on the assumption that the patient has a normal renal function. In patients with impaired renal function, a longer serum concentration interval may be an initial or steady-state period of time in which the drug is not being eliminated in patients with normal renal function. It is appropriate to attempt to reduce the dose of digoxin, such patients are at high toxicity, and toxic effects will last longer in such patients than in patients with normal renal function.

**Interactions with Electrolyte Disorders:** In patients with hypokalemia or hypomagnesemia, toxicity may occur despite serum concentrations below 2 ng/mL, because potassium or mag-

[illegible]

**Pharmacokinetics:** Race differences in virginin pharmacokinetics have been formally studied. Because digoxin is primarily eliminated by the kidney, it is not surprising that there are no differences in creatinine clearance among races; plasma clearance of digoxin to reach an end is not expected. Clearance of digoxin can be primarily correlated with renal function, as indicated by the following evidence. The Cockcroft and Gault formula for estimation of creatinine clearance includes age, sex, and weight. A table that provides creatinine clearance estimates and the corresponding digoxin dose requirements of virginin tablets based on daily administration (Per 70 kg) is presented in the **DISAUGE AND ADMINISTRATION**

used in the degree of activation of the sympathetic nervous system. The vagus nerve is the main parasympathetic outflow system (functional neural deactivation of the vagus nerve results in a high heart rate and decreased conduction velocity). (5) Although the AV node is a potential site of vagal innervation, the effects of vagal stimulation on the AV node are minimal. The effects of vagal stimulation on the AV node are mediated by its positive inotropic and chronotropic effects, whereas the effects of the vagus on the SA node are related to its vagomimetic actions. In high doses, vagal stimulation causes a marked decrease in the heart rate and causes sympathetic outflow from the central nervous system. This is thought to be a protective mechanism to prevent excessive sympathetic activity may be an important feature of vagal stimulation.

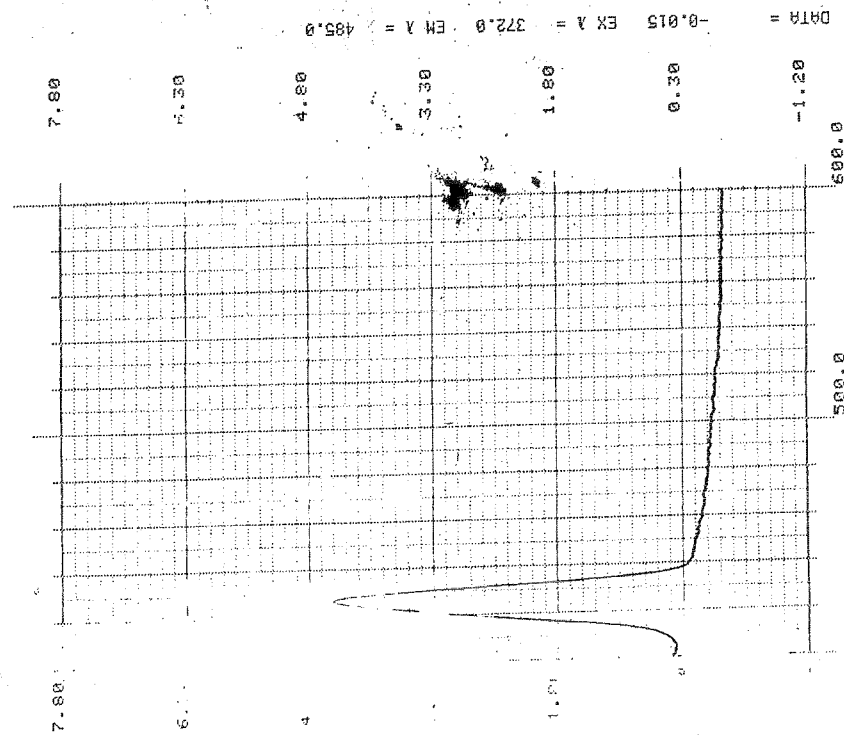
**Effects of vagal stimulation on heart rate, blood pressure, and heart rate variability.** Following oral administration, peak heart rate reductions of 10 to 15 beats per minute (bpm) and reductions of diastolic blood pressure have been demonstrated. The heart rate reduction was more pronounced in patients with a heart rate of 70 to 80 bpm compared to an identical sedation dose of diazepam.

[illegible]

Attachment B Digoxin Tablets (0.125 mg) 4/24/08

Spl. # 448881

Spl. # 448881  
4/24/08 vpw

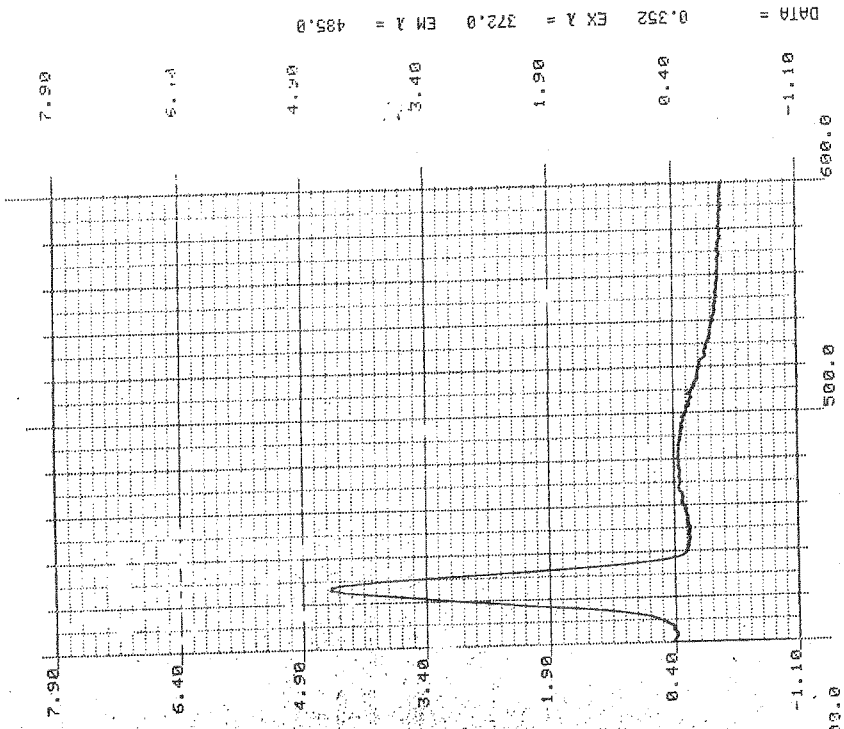


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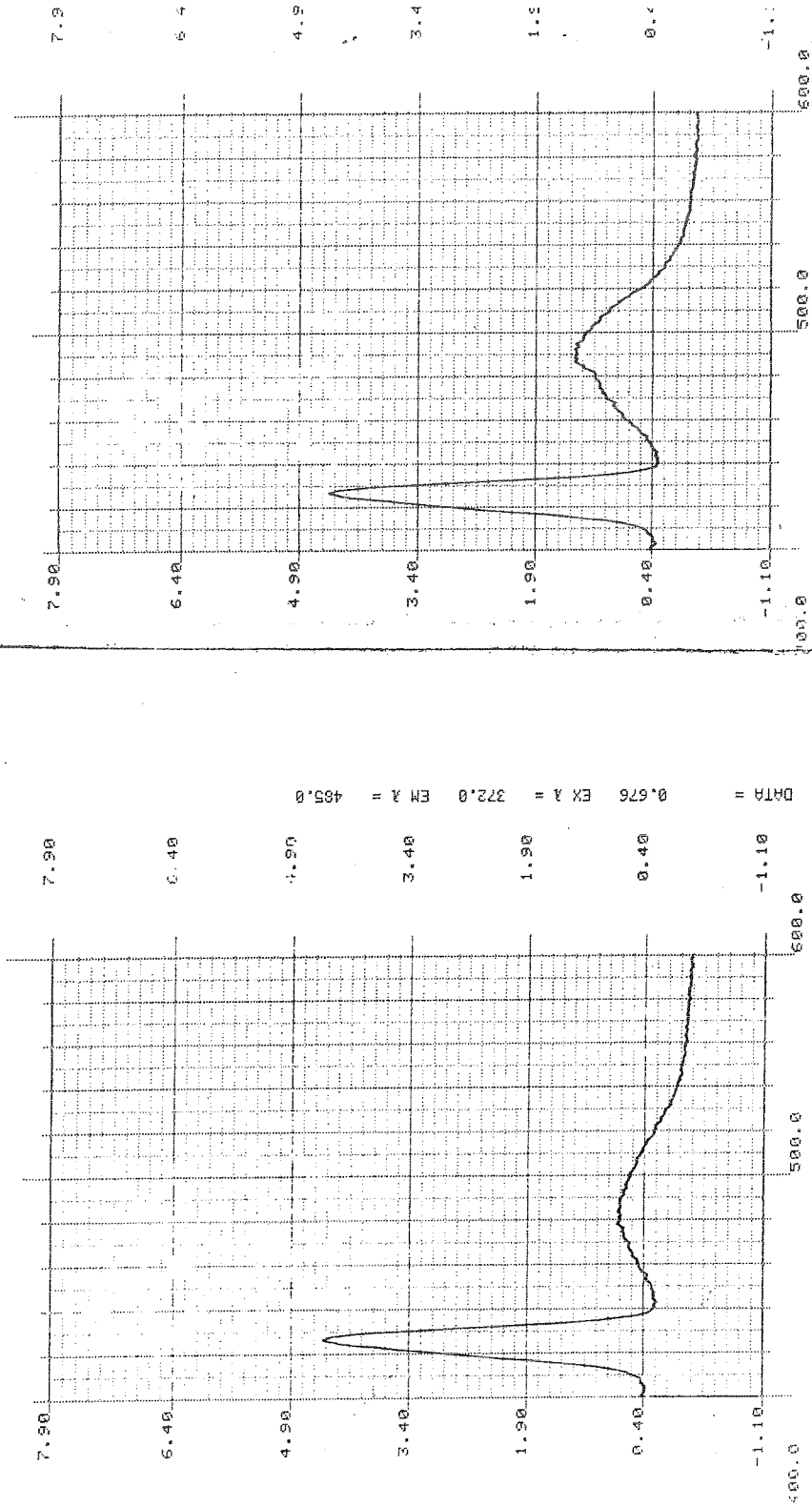
CHART 200-91527

SHIMADZU CORPORATION CHART 200-91527

SHIMADZU CORPO



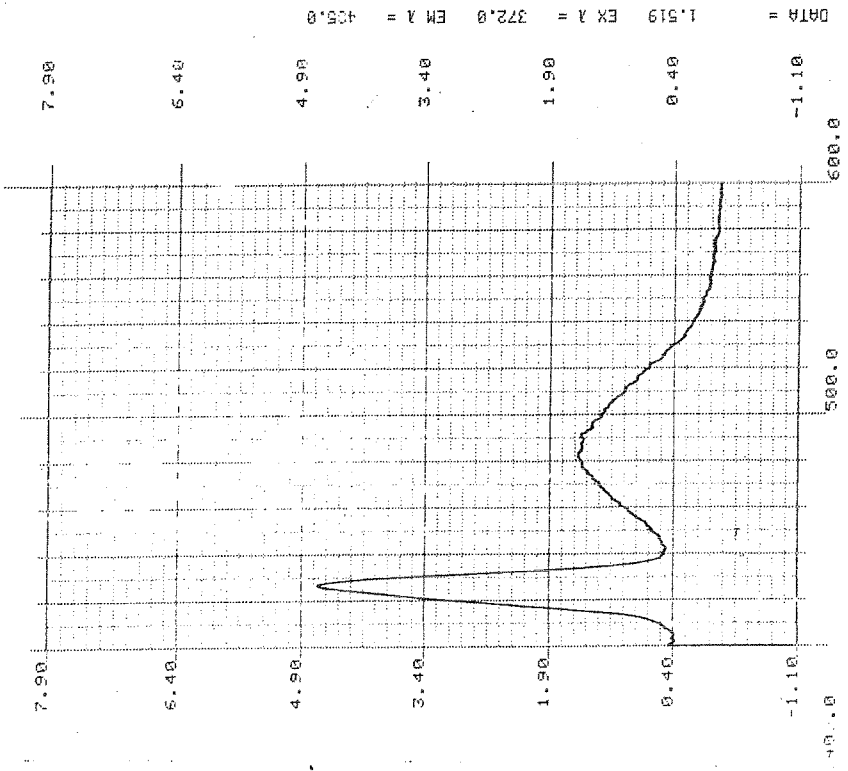
Std 20%



DATA = 0.676 EX A = 372.0 EM A = 485.0

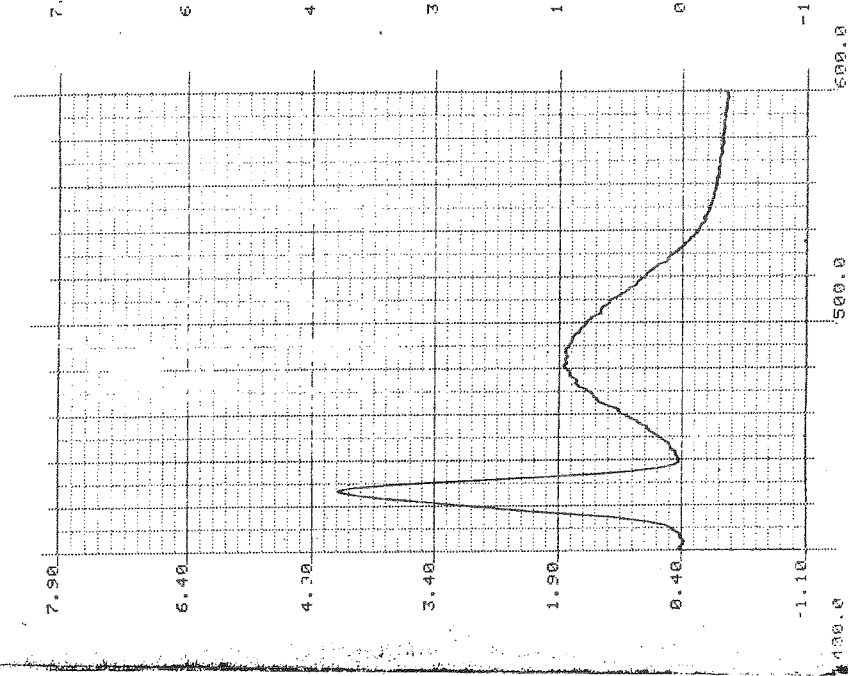
RATION CHART 200-91527

SHIMADZU CORPORATION CHART 200-91527



Std 80%

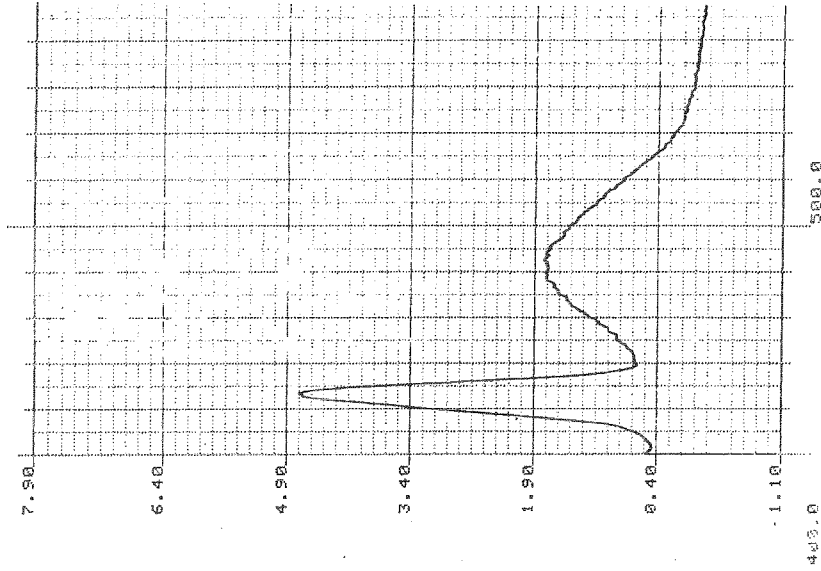
U CORPORATION CHART 200-91527



Std 100%

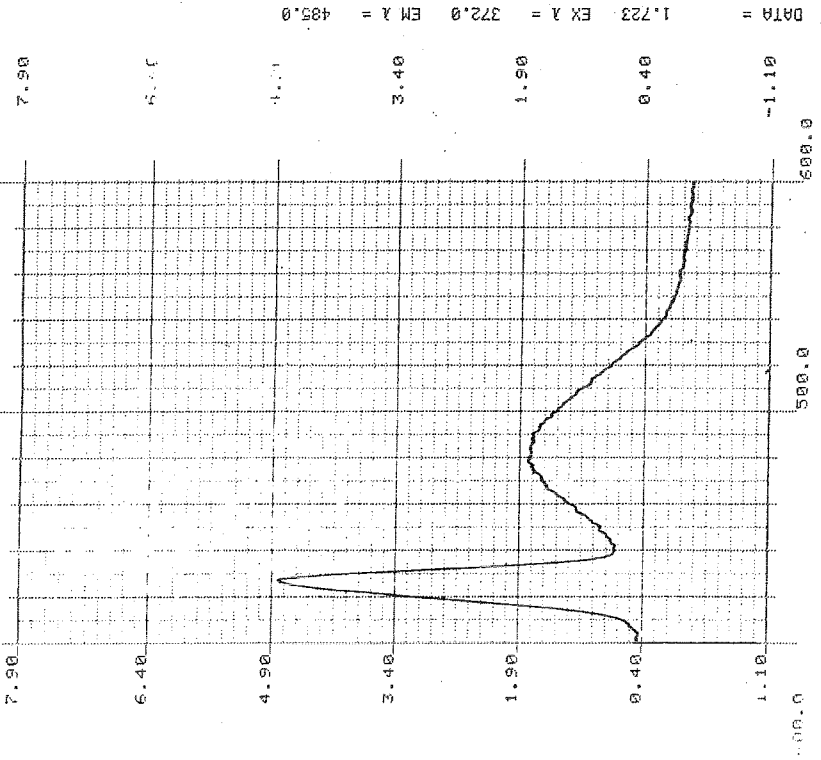
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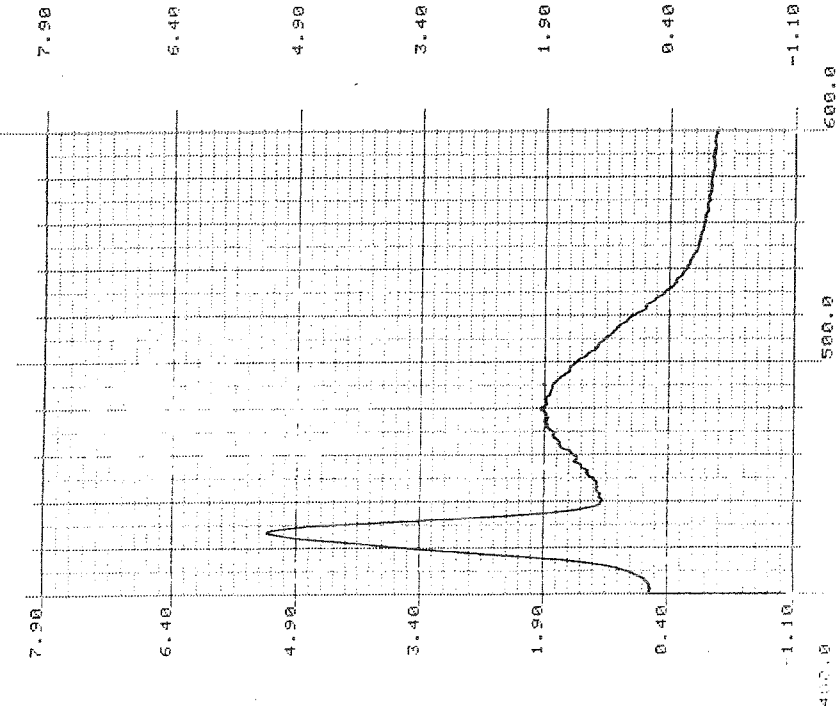
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SHIMADZU CORPORATION CHART 200-91527



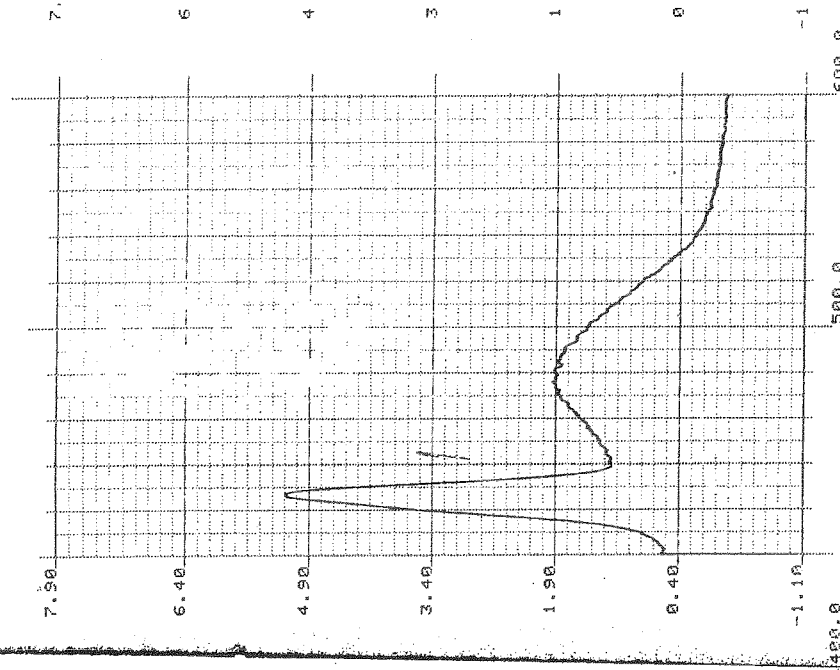
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SHIMADZU CORPORATION CHART 200-91527



Tab 2-1

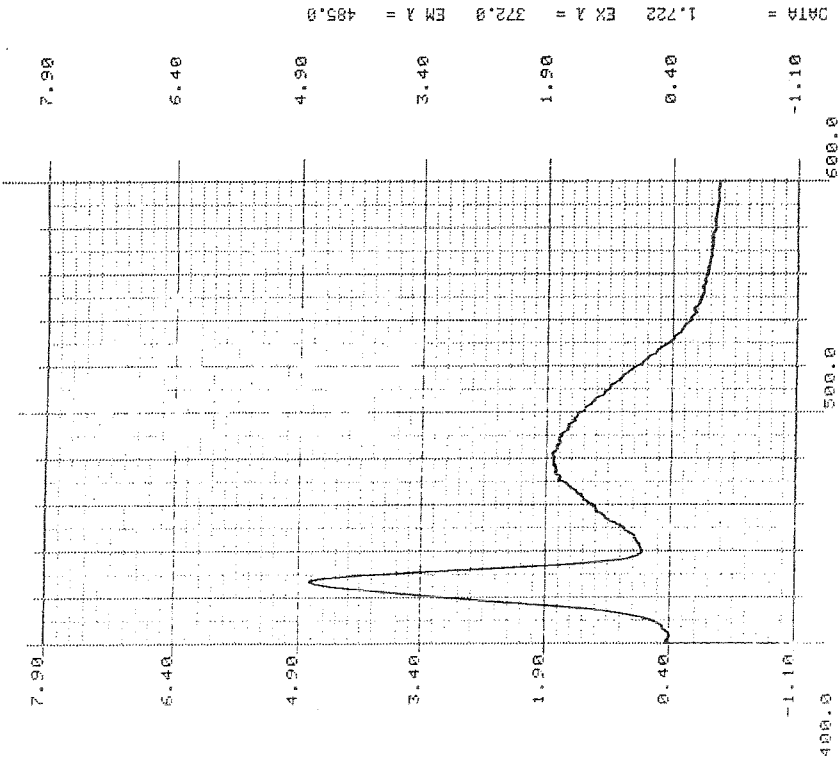
ADZU CORPORATION CHART 200-91527



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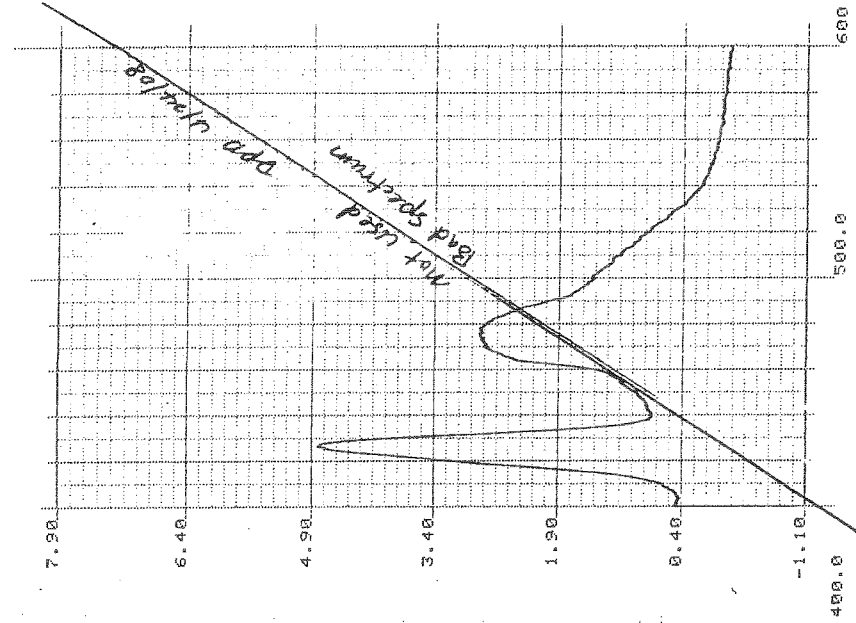
SHIMADZU CORPORATION CHART 200-91527

DATA # 1.829 EX λ = 372.0 EM λ = 485.0



Tab 3-1

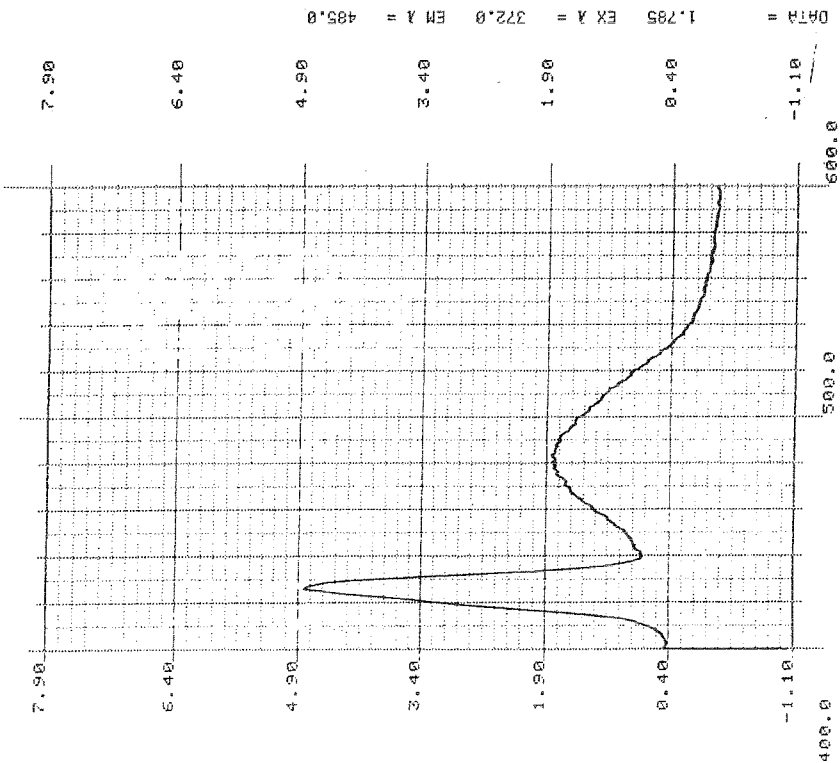
SHIMADZU CORPORATION CHART 200-91527



Not used

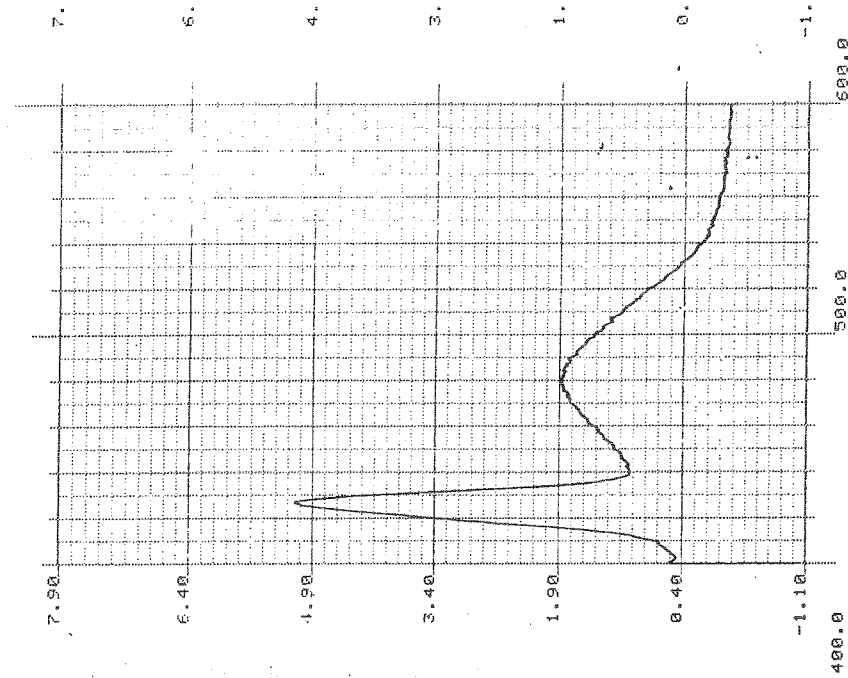
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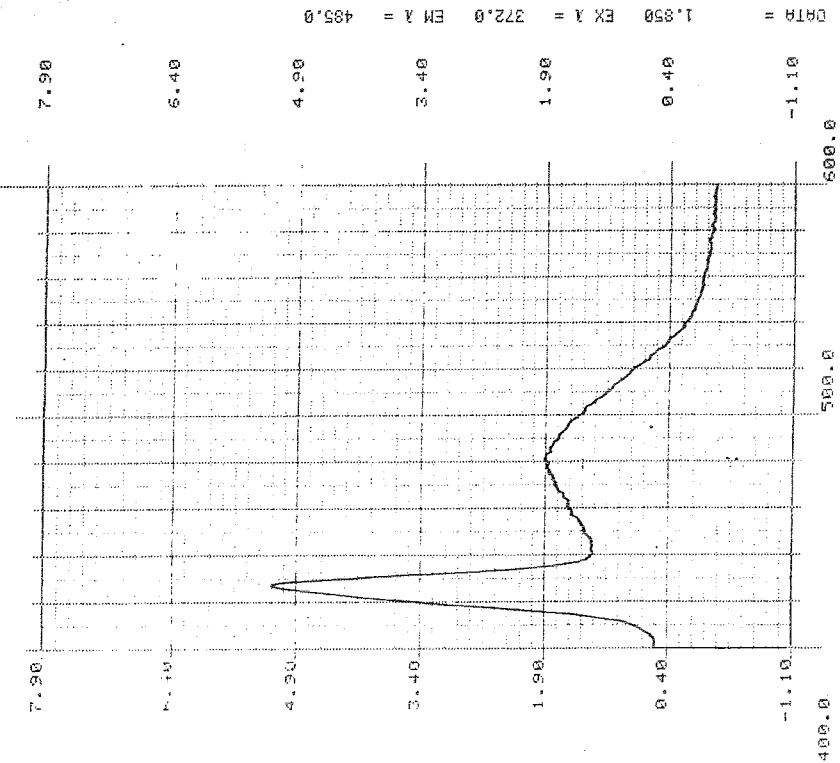
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SHIMADZU CORPORATION CHART 200-91527



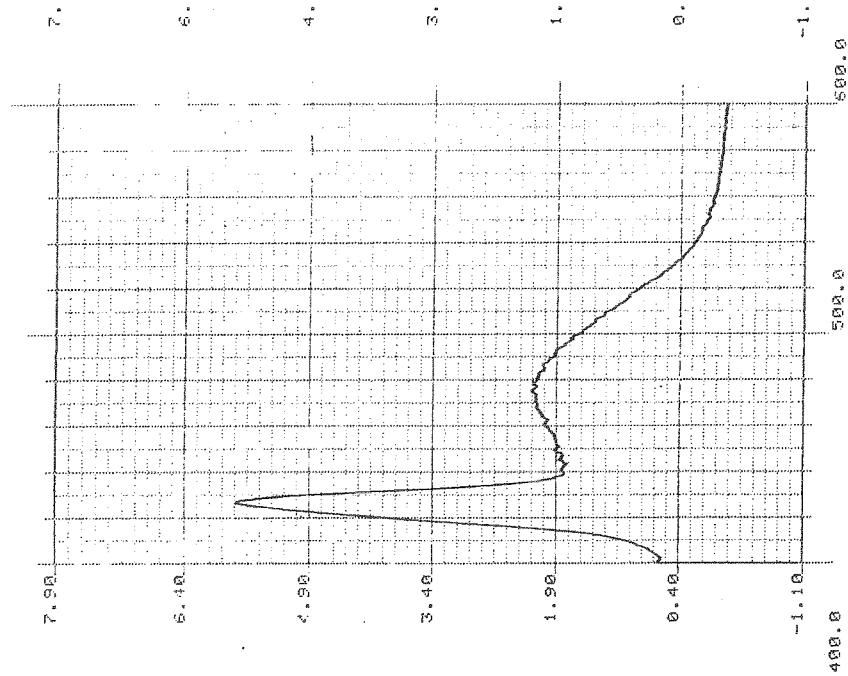
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SHIMADZU CORPORATION CHART 200-91527



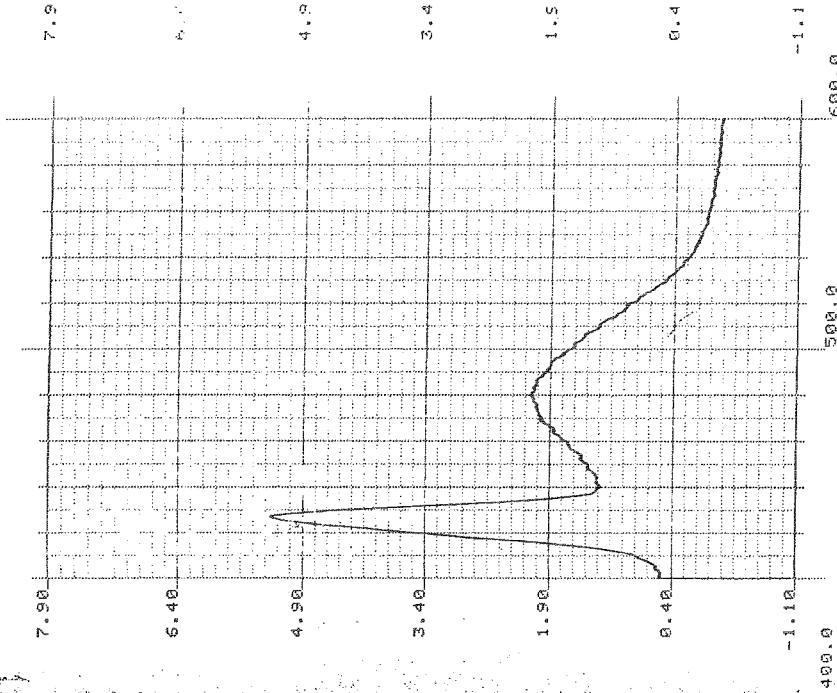
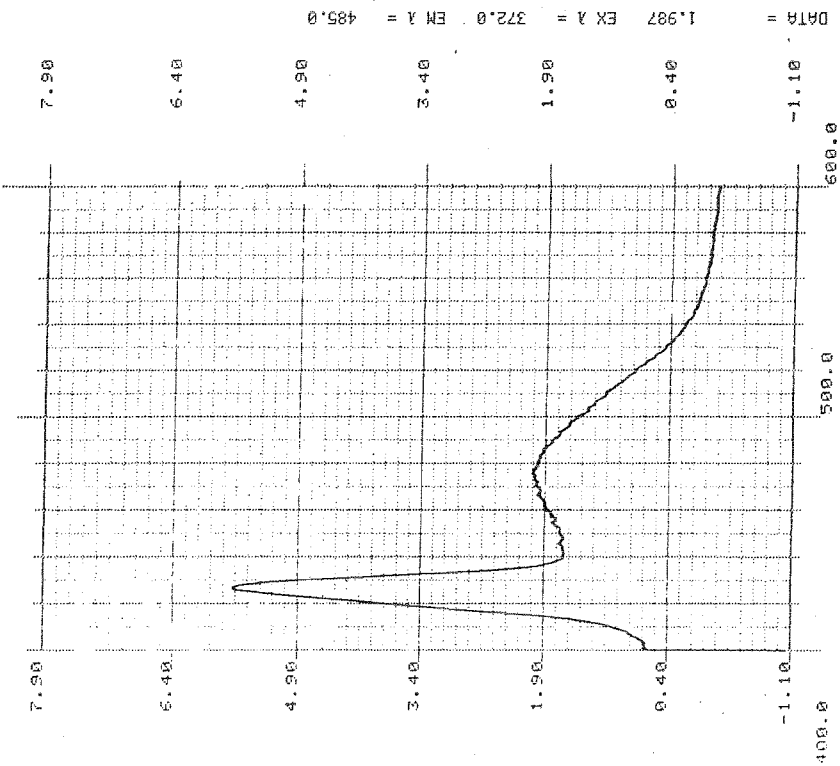
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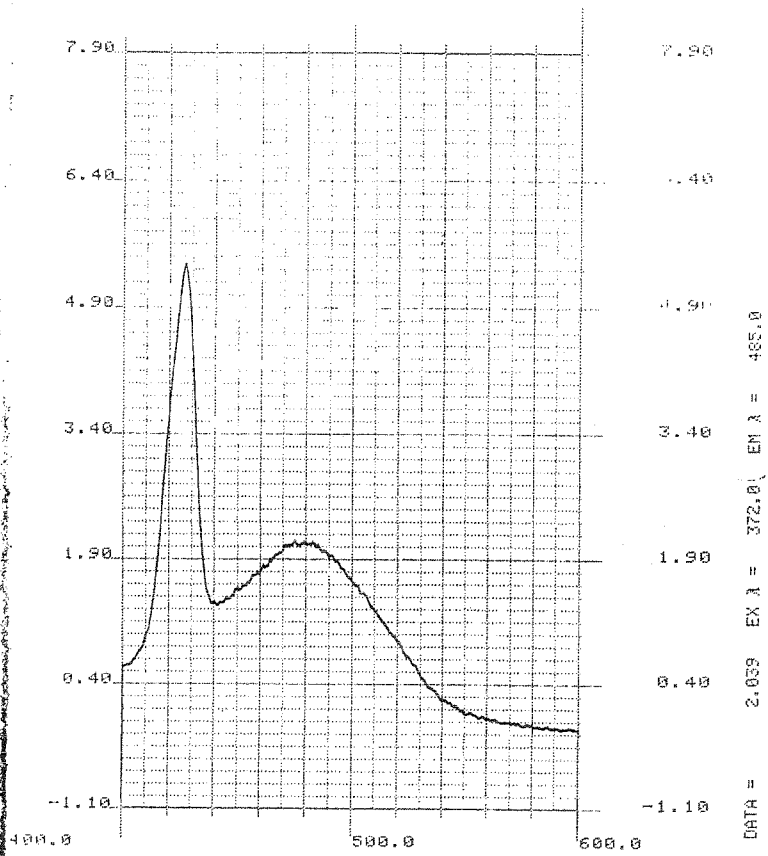
SHIMADZU CORPORATION CHART 200-91527



Tab 5-1

SHIMADZU CORPORATION CHART 200-91527





Tab 6-2

⊕ SHIMADZU CORPORATION CHART 200-91527

# **Food and Drug Administration Office of Regulatory Affairs** **Collection Report**

**For Sample Number: 448881**

This is an accurate reproduction of the original electronic record as of 01/30/2008

<b>Flag</b>	<b>Flag Remarks</b>				
Survey Sample	FY 2008 Low Cost Generic Drug Sample Survey # 2008-800				
<b>Episode Number</b>	<b>Origin</b>	<b>Basis</b>	<b>Sample Type</b>	<b>FIS Smpl Num</b>	<b>Status</b>
	Domestic	Surveillance	Official	0882632	Completed
<b>FEI</b>	<b>Date Collected</b>	<b>Product Code</b>	<b>Responsible Firm</b>	<b>PAC</b>	<b>Hours</b>
1610608	12.03/2007	63FCA06	Shipper	56008A	2
<b>Compliance Num</b>	<b>Country of Origin</b>				
	United States				
<b>Related Smpl Num</b>	<b>Position Class</b>	<b>Sampling District</b>	<b>NDC Number</b>	<b>Permit Number</b>	<b>Storage Rqrmnt.</b>
	INV	DET-DO	62794-145-01		Ambient
<b>Dealer is Consumer</b>	<b>Crx/DEA Schedule</b>	<b>Recall Num</b>	<b>Consumer Compl. Num</b>	<b>Brand Name</b>	
No				Digitek	

**Product Description**

100 x 0.125mg Digoxin Tablets, USP

**Product Label**

See continuation.

**Reason for Collection**

The sample was collected as per memo for the FY 2008 Low Cost Generic Drug Sample Survey # 2008-800 (CP 7356.008) and is being reported in FACTS under Assignment # 896688 and Op # 3518058.

**MFG Codes**

70298A1

**Expiration Date**

April 2009

<b>Firm Legal Name</b>	<b>Address</b>	<b>Type of Firm</b>	<b>Firm FEI</b>	<b>FCE</b>
UDL Laboratories, Inc	12720 Dairy Ashford Rd Sugar Land, TX 77478-2844 US	Shipper	1610608	
Actavis Totowa LLC	101 E Main St Little Falls, NJ 07424-5608 US	Manufacturer	2244683	
Wal-Mart Pharmacy Warehouse #6028	801 Corda Blvd Crawfordsville, IN 47933-2152 US	Dealer	3004344335	
<b>Size of Lot</b>	<b>Est. Value</b>	<b>Rcpt Type</b>	<b>Carrier Name</b>	<b>Date Shipped</b>
(b) (4) 100 count bottles		FDA484		

**Description of Sample**

See continuation.

**Method of Collection**

2 x 100 count bottles of Digitek (Digoxin Tablets, USP) lot 70298A1 were randomly selected from shelf.

**How Prepared**

See continuation.

**Collector's Identification on Package and/or Label**

"Sample # 448881 EB 12/3/07"

**Collector's Identification on Seal**

"448881 Ernest Bizjak 12/3/07"

**Sample Delivered To**

FEDEX

**Date Delivered**

12/17/2007

**Orig C/R & Records To**

DAL-DO

**Lab w/Split Sample**

0

**Lab**

NRL

**Document Number**

**Document Date**

12.03/2007

**Document Type**

Other

**Document Remarks**

FDA-482; 1 page

Date: 01.30/2008

Page: 1 of 3

**Food and Drug Administration Office of Regulatory Affairs**  
**Collection Report**

**For Sample Number: 448881**

This is an accurate reproduction of the original electronic record as of 01/30/2008

12/03/2007

Other

FDA-484; 4 pages

**Remarks**

See continuation.

**Payment Amount**

**Payment Method**

No Charge

**704(d) Sample**

No

**702(b) Portion**

No

**Collector's Name**

Ernest Bizjak

**Name of Signer**

Ernest Bizjak

**Date & Time of Signature**

12/14/2007

09:12 AM

ET

**Meaning**

Collector

**Food and Drug Administration Office of Regulatory Affairs  
Collection Report**

**For Sample Number: 448881**

This is an accurate reproduction of the original electronic record as of 01/30/2008

**Continuation:**

**Product Label**

The white HDPE bottles with matching screw caps are labeled in part "NDC 62794-145-01 \*\*\* DIGITEK \*\*\* (digoxin tablets, USP) 125 mcg (0.125mg) \*\*\* 100 TABLETS \*\*\* Rx only \*\*\* Distributed by: BERTEK PHARMACEUTICALS INC. Sugar Land, TX 77478 USA \*\*\* Manufactured by: AMIDE PHARMACEUTICALS, INC. 101 East Main Street Little Falls, NJ 07424 USA \*\*\* Control No.: 70298A1 \*\*\* Exp. Date: APR 09".

**Description of Sample**

The sample consists of 2 x 100 count bottles 0.125mg Digitek (Digoxin Tablets, USP) NDC # 62794-145-01 assigned lot # 70298A1 and expiry date April 2009.

**How Prepared**

The 2 bottles were identified as per Collector's ID and placed into a clear Whirl-pak bag that was then officially sealed at the dealer. The sample was transported back to the DET-DO/INDY-RP where it was stored in a locked sample cabinet at ambient conditions until it was boxed and shipped to lab.

**Remarks**

Per assignment memo, test samples for UDU, Diss, and ID. All analytical methods are compendial.

Dena McClamroch, General Manager stated that she could not provide a dollar value for the sample. If this information is needed, contact Monty Mason, Pharmacy Director at ph#479-277-1558.